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# ARCHIVES OF SURGERY

VOLUME 57

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SUPPLEMENT 1

## EFFECTS OF CURTAIN OPERATIONS ON THE ESOPHAGUS OF THE DOG

EXCLUDING ESOPHAGEAL OBSTRUCTION AND COMPLETE  
ESOPHAGEAL FISTULA

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CLEVELAND

The important observation by Haden and Orr<sup>1</sup> in 1923 that obstruction of the esophagus or of the cardiac end of the stomach in the dog is rapidly fatal has been confirmed by Wangensteen and Chunn.<sup>2</sup> Such animals die in from thirty-six to seventy-two hours if untreated. In view of the great significance of these observations further study has seemed worth while in an attempt to procure more data regarding the abnormal physiology concerned in the lethal outcome.

### METHODS

All operations were performed under ether anesthesia after the preliminary administration of atropin (0.016 Gm) or morphine sulphate hypodermically. The morphine caused emesis and purging. Samples of blood were drawn before operation and at subsequent intervals and determinations of the blood chlorides, the carbon dioxide combining power of the plasma, the blood urea nitrogen and, in some cases, of the blood sugar were carried out. The animals were not given any food or water except as indicated in the accompanying tables. In certain experiments the rectal temperature was taken before operation and daily thereafter. All dogs were kept in cages, and the amount of urine and feces observed. The excreta were scanty, however, and after careful measurement and analysis in a few cases further collection was abandoned as the data obtained were not significant. A series of animals were weighed before operation and after death, and the loss of weight was noted. Postmortem examinations were performed, and all animals discarded from the series in which an obvious cause of death other than esophageal obstruction such as empyema, pneumonia or mediastinitis, was demonstrable.

In order to make the operations similar in as many cases as possible the following procedure was used in most instances. An ordinary wooden spool was whittled into an hour-glass shape, and the hole through the middle enlarged to permit the insertion of a thin-walled, nickel tube about 1 cm. in diameter, which projected for a distance of about 1 inch from the lower end of the spool. In order to

\* Submitted for publication, Sept. 3, 1929.

\* From the Laboratory of Experimental Surgery, Department of Surgery, University of Cincinnati College of Medicine.

1 Haden, R. L., and Orr, T. G. *J. Exper. Med.* **38**: 477, 1923.

2 Wangensteen, O. H., and Chunn, S. S. *Studies in Intestinal Obstruction*, Arch. Surg. **16**: 1242 (June) 1928.

produce obstruction, the hole in the spool was plugged with wood, and for the production of esophageal fistula a soft-walled rubber tube of large caliber was attached to the nickel tube projecting from the spool, and was brought out through a tangential gastrostomy opening. In other cases the spool with the short nickel tube inserted was ligated in the esophagus, permitting the passage of saliva into the stomach, the animals, however, having been subjected to operations of practically the same magnitude as in the cases of obstruction and fistula.

#### EFFECTS OF SIMPLE ESOPHAGEAL OBSTRUCTION

In six animals the esophagus was completely obstructed five times in the cervical region and once just above the diaphragm. The animals invariably died. The average duration of life was fifty-three hours, the extremes being forty-eight and seventy-two hours. Table 1 shows the data obtained from this series.

The changes noted in the blood were a fall in blood chlorides, a slight decrease in the alkali reserve and a considerable rise in the blood urea. The weight lost by such animals averaged 9 per cent.

TABLE 1—*Effects of Esophageal Obstruction (Six Animals)*

	Average	Lowest	Highest
Duration of life	53 hours	48 hours	72 hours
Blood chlorides before operation	457	363	620
Blood chlorides just before death	351	211	600
Carbon dioxide combining power before operation	39	30	47
Carbon dioxide combining power just before death	36	24	40
Urea nitrogen before operation	9	8.3	14
Urea nitrogen just before death	62.1	11.1	130
Loss of weight	9%		

#### EFFECTS OF ESOPHAGEAL FISTULA

While Pavlov<sup>3</sup> and others<sup>4</sup> have reported that animals with esophageal fistulas can be kept alive if a previous gastrostomy is performed for feeding purposes, Jackson<sup>5</sup> in 1923 called attention to the fact that patients fed through gastrostomy do much better if their saliva is admixed with the food. This fact is now widely acknowledged by clinicians.

For the purpose of comparison with the effects of esophageal obstruction and in order to note the results of esophageal fistula without food or fluids, fistulas were established in seven animals. In three, the fistula was made in the neck by dividing the esophagus, inverting the lower end and bringing out the upper end through a stab wound to the left of the midline incision. In four, the procedure already described,

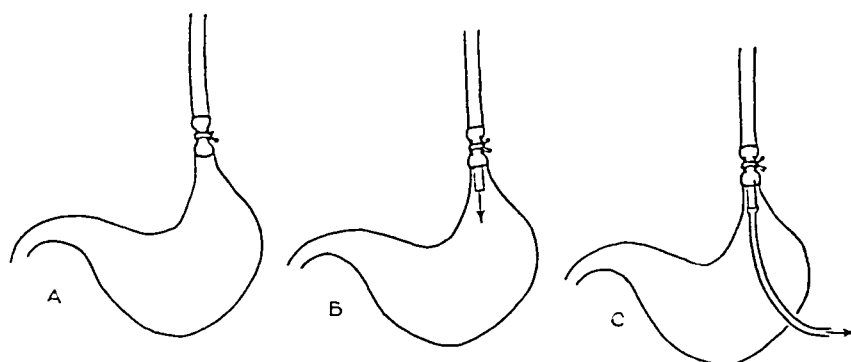
3 Pavlov, J. P. *Handbuch der physiologischen Methodik*, 1908, vol. 2, part 2.

4 Pavlov, J. P., and Schumowa-Simonowskaja. *Arch. f. Anat. u. Physiol.*, 1895.

5 Jackson, Chevalier. *Arch. Pediat.* 40:324, 1923.

the ligation of a hollow spool with a tube attached in the thoracic esophagus bringing the tube out through a gastrostomy opening was employed. In these experiments also the animals invariably died. The effects of esophageal fistula are shown in table 2.

The average duration of life was somewhat longer than in the animals with obstruction, being seventy-three hours. One dog died in thirty-six hours while one lived ninety-six hours, and one 144 hours. The blood chlorides were not so strikingly decreased as in the animals with esophageal obstruction falling below normal limits in only one animal. The alkali reserve of the blood, however, was more profoundly affected, an average fall of 10 per cent by volume in the plasma carbon dioxide capacity (25 per cent of the average preoperative value) being noted. The blood urea rose above normal limits in only one animal of the



4, esophageal obstruction. Solid spool ligated in the thoracic esophagus. B, hollow spool ligated in the thoracic esophagus. C, esophageal fistula. Tube attached to hollow spool brought out through gastrostomy.

TABLE 2—Effects of Esophageal Fistula (Seven Animals)

	Average	Lowest	Highest
Duration of life	73 hours	36 hours	144 hours
Blood chlorides before operation	589	429	670
Blood chlorides just before death	520	321	625
Carbon dioxide combining power before operation	40	29	46
Carbon dioxide combining power just before death	39	18	40
Urea nitrogen before operation	11.5	9.5	20
Urea nitrogen just before death	19.5	9.0	42.7
Rectal temperature before operation	98.8	98	99.6
Highest temperature after operation	101.2	100	104.6
Loss of weight	16%	7%	28%

series. Loss of weight was a more prominent feature with fistula than with obstruction, the average loss of weight being 16 per cent of the preoperative weight, and the extremes being 7 per cent and 28 per cent. No marked temperature changes were noted, the average rectal temperature before operation being 98.8 while the average highest



temperature before death was 101.2. In one animal, the rectal temperature reached 104.6 just before death.

#### EFFECTS OF LIGATION OF THE ESOPHAGUS AROUND A HOLLOW SPOOL

In order to determine the effect of ligation of the esophagus around a hollow spool placed in the lumen of this structure, this operation was performed in two animals. One of these lived seven days and one eleven days, both dying of empyema and mediastinitis caused by leakage from the esophagus due to the tape having cut through the wall. These animals exhibited little change in the chemical composition of the blood as indicated in table 3. The rise in temperature, and indeed the ultimate lethal outcome, can well be explained on the basis of the complicating infection. It is significant, however, that with an average duration of life of nine days the average loss of weight was only 11.5 per cent, or about the same amount as seen in the cases of obstruction in which the

TABLE 3—*Effects of Ligation of a Hollow Spool in Thoracic Esophagus (Two Animals)*

	Average	Lowest	Highest
Duration of life	9 days 216 hours	7 days 168 hours	11 days 264 hours
Blood chlorides before operation	615	610	620
Blood chlorides just before death	610	605	615
Carbon dioxide combining power before operation	38.5	33	44
Carbon dioxide combining power just before death	31.5	27	36
Highest temperature after operation	104.3	103.8	104.8
Loss of weight	11.5%	9%	14%

Ligatures cut through and dogs died of mediastinitis, empyema and pneumonia

animals lived only forty-eight hours, and considerably less than in the animals with esophageal fistula in which the average duration of life was seventy-three hours.

#### EFFECTS OF ESOPHAGEAL OBSTRUCTION FOLLOWED BY THE INJECTION OF SODIUM CHLORIDE

Haden and Orr<sup>6</sup> have reported that animals in which ligation of the cardiac end of the stomach had been performed could be kept alive for thirty-two days or more if given sufficient amounts of sodium chloride (40 cc per kilogram) after operation.<sup>7</sup> In three animals we have produced a complete esophageal obstruction and then injected 40 cc per kilogram of 1 per cent sodium chloride hypodermically each day including the day of operation (table 4). The duration of life

<sup>6</sup> Haden, R. L., and Orr, T. G. J. Exper. Med. 48: 627, 1928.

<sup>7</sup> Haden and Orr (footnote 1, p. 479) state, regarding the dogs with ligation of the cardiac end of the stomach, that "in no animal was the cardiac opening completely occluded. In most instances a lead pencil could be passed through."

in these animals was not prolonged. The alkali reserve fell about 16 per cent by volume, but the blood urea nitrogen remained within normal limits. While some fall in the blood chlorides was noted, it did not reach a point significantly below normal limits. An average rise of 1 degree in the rectal temperature was noted. The average loss of weight in these animals was 9 per cent.

#### EFFECTS OF ESOPHAGEAL OBSTRUCTION FOLLOWED BY THE INJECTION OF SODIUM CHLORIDE AND SODIUM BICARBONATE

Because of the invariable decrease in the alkali reserve in the animals of this series often to a point well below normal limits, esophageal

TABLE 4—*Effects of Obstruction of the Esophagus Combined with the Administration of Forty Cubic Centimeters of Two-Tenths Saline per Kilogram, Four Times Daily (Three Animals)*

	Average	Lowest	Highest
Duration of life	43 hours	40 hours	48 hours
Blood chlorides before operation	549	402	625
Blood chlorides just before death	550	430	615
Carbon dioxide combining power before operation	37	28	42
Carbon dioxide combining power just before death	21	18	24
Urea nitrogen before operation	9.9	6.7	13
Urea nitrogen just before death	10.5	10	11
Rectal temperature before operation	100.7	99	102.5
Highest temperature after operation	101.7	99.2	104.2
Loss of weight	9%		

TABLE 5—*Effects of Esophageal Obstruction Combined with the Administration of Two-Tenths Normal Saline Forty Cubic Centimeters per Kilogram and Sodium Bicarbonate One Gram per Kilogram Daily (Five Animals)*

	Average	Lowest	Highest
Duration of life	46 hours	24 hours	80 hours
Blood chlorides before operation	574	550	580
Blood chlorides just before death	614	605	622
Carbon dioxide combining power before operation	43	37	54
Carbon dioxide combining power just before death	39	34	47
Rectal temperature before operation	100.5	100.2	100.8
Highest temperature after operation	102.7	100.6	106.4
Loss of weight	11%		

obstruction was produced in five animals and 40 cc of 1 per cent sodium chloride and 1 Gm of sodium bicarbonate per kilogram of body weight were injected each day after operation. These measures also failed to prolong life, although no significant fall in blood chlorides or alkali reserve values were noted.

#### THE EFFECTS OF COMPLETE FOOD AND WATER STARVATION ALONE

Since except as has been indicated none of the animals with experimental esophageal obstruction received any food or water it was con-

sidered advisable to follow up animals under conditions of complete food and water starvation. Three animals, therefore, were anesthetized with ether for one hour and then kept in cages without food or water. Administration of water was begun after twenty-three days in two animals; the third was allowed to die without fluids or food. These animals lived for twenty-three days or more, one surviving for thirty-two days. Some decrease of blood chlorides occurred in two of the dogs, and all showed a fall in the alkali reserve. A terminal rise of the blood urea nitrogen as noted by Bacon, Anslow and Eppler<sup>8</sup> in their studies on dehydration was observed in the single animal allowed to die.

Several other control experiments were performed. In one animal all of the vagus branches were sectioned just above the diaphragm and the esophageal wall itself divided down to the submucosa. This animal was not given any food or water for ten days, but was in good condition at the end of that time. Food and water were then permitted, and the animal was followed up for ninety days, at the end of which time he

TABLE 6—*Effects of Water and Food Starvation (Three Animals)*

	Average	Lowest	Highest
Duration of life	23 days+		32 days
Blood chlorides before operation	437	425	462
Blood chlorides just before death	445	313	518
Carbon dioxide combining power before operation	47	35	52
Carbon dioxide combining power just before death	36	26	42
Urea nitrogen before operation	12	8	17
Urea nitrogen just before death	24	6	42

did not show any ill effects. The chemical composition of the blood exhibited no significant changes during that time.

Division of the cervical esophagus with immediate end to end anastomosis was not followed by any ill effects, except a fall in blood chlorides of 34 per cent. The animal recovered completely.

#### SUMMARY

The striking result of these experiments is that dogs invariably die following the sudden and complete obstruction of the esophagus, also, the production of esophageal fistula without subsequent administration of fluids was invariably followed by death in the animals of this series. The cause of death in these animals is not clear. Dehydration, while it may play a rôle, is not the sole agent, as evidenced by the fact that animals can live for thirty days or more when food and water are entirely withheld. Further, animals dying with esophageal obstruction do not exhibit the terminal rise in temperature usually seen in animals dying from dehydration.

<sup>8</sup> Bacon, D. K., Anslow, R. E., and Eppler, H. H. Intestinal Obstruction, Arch. Surg. 3: 641 (Nov.) 1921.

The studies of the changes in the chemical composition of the blood in this series indicate a tendency toward a decrease in the carbon dioxide combining power of the plasma and in the chlorides of the blood in some animals, but these changes are not constant. The blood urea nitrogen showed a terminal rise in a few instances. The average duration of life following the production of esophageal fistula and without the administration of fluids was seventy-three hours, one animal living for six days.

We have not been able to increase materially the duration of life in animals with esophageal obstruction by the administration of sodium chloride, or of sodium chloride and sodium bicarbonate.

The fact that animals with esophageal fistulas die in almost as short a time as those with esophageal obstruction, and apparently in a similar manner, suggests that the loss of saliva may play an important rôle in the lethal outcome. Studies are now being made with regard to this point.

# LIVER AUTOLYSIS IN VIVO<sup>†</sup>

JAMES C ELLIS, MD

AND

LESTER R DRAGSTEDT, MD

CHICAGO

The question of the effect of in-vivo autolysis of tissues has been reopened by the recent reports of Mason, Davidson, Matthew and Rastello,<sup>1</sup> Wangenstein and Waldron<sup>2</sup> and Haden and Orr<sup>3</sup> that the aseptic autolysis of small portions of liver in vivo is uniformly fatal in dogs. This conclusion was reached following the finding that the ligation of a lobe of the liver in the dog or the placing of a free portion of dog's liver, obtained with strict aseptic precautions, in the general abdominal cavity regularly caused death in from fifteen to sixty hours. In 1917, Dragstedt, Moorhead and Burcky<sup>4</sup> reported that the in-vivo autolysis of short, isolated sections of intestine that had been sterilized by prolonged drainage into the peritoneal cavity did not produce any serious effect in dogs. When such segments were infected, however, death followed shortly after the occlusion of their blood supply. In 1921, and later, we found that a similar situation obtained in the case of the spleen and the kidney. When these organs were sterile, a ligation of the blood supply with resulting necrosis and absorption was without effect in dogs, but it caused death when these organs were infected. The presence of gas-forming anaerobes was more fatal than that of other organisms. In the experiments with so-called aseptic autolyzing liver, the observers commented on the formation of gas in the necrotic tissue.

The question of the formation of highly toxic substances from body tissues through hydrolytic decomposition brought about by intracellular

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<sup>†</sup> From the Department of Surgery of the University of Chicago

<sup>‡</sup> This work has been done under a grant from the Douglas Smith Foundation for Medical Research

1 Mason, E C, Davidson, E C, Matthew, C W, and Rastello, P B. Tissue Autolysis in Vivo. I. Blood Changes. Physical and Chemical, *J Lab & Clin Med* **10** 622, 1924. A Study of Tissue Autolysis in Vivo. II. A Pharmacological Study of the Toxic Material, *J Lab & Clin Med* **10** 906, 1924

2 Wangenstein, O H, and Waldron, G W. Studies in Intestinal Obstruction. IV. Strangulation Obstruction, *Arch Surg* **17** 430 (Sept) 1928

3 Haden, R L, and Orr, T G. The Blood Chlorides in Proteose Intoxication, *J Exper Med* **48** 639, 1928

4 Dragstedt, L R, Moorhead, J J, and Burcky, F W. Intestinal Obstruction. An Experimental Study of the Intoxication in Closed Intestinal Loops, *J Exper Med* **25** 421, 1917

enzymes is of great practical and theoretical interest. For the most part, the development of toxicity in autolysates conducted in vitro has been produced by contaminating bacteria. In-vivo autolysis of varying amounts of tissue probably occurs after every surgical operation, the degree depending on the amount of tissue left within the grasp of ligatures. Many surgeons have commented on the hazard of leaving dead tissue in wounds, and in particular have stressed the disastrous effect of infection in such cases.

TABLE 1—*The Effect of Ligating a Lobe of the Liver and Leaving It in Place*

Dog	Procedure	Length of Life Hr	Effect on Nonprotein N, Urea N and NaCl in Blood	Observations at Autopsy	Remarks
230	Left lobe of liver ligated (approximate weight of liver 75 Gm)	Less than 20	None	Ligated lobe of liver necrotic gray and spongy some chocolate fluid in the abdomen	
282	Left lobe of liver ligated (approximate weight of liver 75 Gm)	Less than 20	None	Ligated lobe of liver soft, gray and spongy about 250 cc of pure blood in the peritoneal cavity	Hemorrhage around the ligature
339	Small lobe on left side of liver ligated	Less than 24	NaCl fall 100 mg per 100 cc of blood NPN and Urea N Unchanged	Ligated lobe of liver slightly darker than the rest about 300 cc of blood in the peritoneal cavity	Perhaps a death from hemorrhage
334	Small lobe on left side of liver ligated	20	None	Ligated lobe of liver gray-brown mushy and full of gas bubbles loops of intestines about the lobe showed in jection	
345	Small lobe on left side of liver ligated at its base with cat gut	20	None	50 cc of thick chocolate brown fluid in the abdomen periphery of the ligated lobe of liver dark brown spongy containing gas periphery nearly normal	Spore bearing anaerobic bacillus cultured from the liver at necropsy apparently not <i>B. welchii</i>

In the following experiments, an attempt has been made to determine the rôle of bacteria in the rapid death produced by liver autolysis in vivo. All experiments were performed on dogs under complete ether anesthesia. In series 1, consisting of five dogs, the small left lobe of the liver was ligated with strict aseptic precautions, the lobe was left in place, and the abdomen closed. All the animals died in less than twenty-four hours. In every instance, the ligated lobe of liver at autopsy was grayish brown, soft and spongy and contained gas. Cultures secured in one instance revealed an anaerobic gram-positive bacillus in the necrotic liver. Detailed protocols are given in table 1.

In series 2, a somewhat different procedure was employed. The abdomen was shaved and scrubbed with soap and water, according to the usual technic. A solution of 95 per cent phenol was then applied, allowed to remain for a minute or two, and then removed with alcohol. The abdomen was then opened by a long midline incision, and the knife discarded. The wound was widely retracted, and sterile clamps were introduced and placed on the common bile duct and the portal vein, respectively. Lobes of liver were then excised with forceps and scissors, care being taken that the liver tissue should come in contact with the gloved hand of the operator as little as possible. Small pieces of liver were immediately transferred to sterile Petri dishes. Cultures were made in plain broth, and to secure the growth of anaerobic forms, pieces of liver were dropped into long tubes containing skimmed milk with bromocresol purple and in others with egg-meat-broth mediums. These tubes had been previously heated to drive off the air, then cooled, inoculated and sealed with vaseline. The broth cultures remained sterile. In both the milk and egg-meat mediums, growth was obtained in forty-eight hours, as a rule. This was a gram-positive bacillus, and it was obtained from all anaerobic cultures of the fresh uncontaminated livers of the four living dogs of this series. The organism was not definitely identified, but had the following characteristics. It was a slender rod with spores at one or both ends, stained by Gram's method but better with Loeffler's methylene blue, formed medium-sized colonies with a marked zone of hemolysis on blood agar plates incubated in desiccators from which the air had been almost completely exhausted, produced gas when grown on meat, produced acid, gas and coagulation in milk, the clot being somewhat liquefied, and was a strict anaerobe. It was not identical with *Bacillus welchii*, though similar in some respects. After cultures had been made of the freshly removed liver, pieces weighing 70 and 80 Gm. were placed in the free abdominal cavities of two normal dogs. Both animals died within thirty hours. In both cases, the transplanted liver was necrotic, friable and spongy with gas. The same gram-positive, anaerobic bacillus was cultured from this tissue. In another dog, a piece of liver (100 Gm.) was introduced between the muscles of the abdominal wall, and the wound tightly closed. A subcutaneous abscess immediately formed and discharged through the skin. The animal survived. The protocols are summarized in table 2.

The experiments detailed demonstrate that the uncontaminated liver of normal living dogs regularly contains anaerobic bacteria. To determine the significance of these organisms in in-vivo autolysis of liver, the following experiments were performed. Two portions of fresh, uncontaminated dog's liver which on culture yielded the gram-positive anaerobic bacillus were sterilized in the autoclave at 15 pounds (6.8 Kg.)

pressure for fifteen minutes. Subsequent cultures gave no growth. These autoclaved portions of liver, weighing 100 Gm each, were placed in the free abdominal cavities of two normal dogs. These dogs showed no subsequent ill effects. One was reoperated on in fifteen days and the portion of liver found to be only about half digested and absorbed. No trace of the transplanted liver was discovered in the abdomen of the second dog at the end of thirty-eight days. It is interesting to note

TABLE 2—*The Effect of Placing Fresh Liver from Another Dog into the Peritoneal Cavity or Muscle Spaces*

Dog	Procedure	Weight of Liver, Gm	Length of Life	Effect on Non-protein N, Urea N and NaCl in Blood	Bacteria of Fresh Liver	Bacteria of Liver at Autopsy	Observations at Autopsy
726	Fresh liver from another animal placed in peritoneal cavity, a piece of the liver being taken for culture first	80	Less than 22 hours	None	Gram positive anaerobic bacillus cultured; broth culture negative	Gram positive anaerobic bacillus in liver substance; cocci in broth culture	Purulent fluid in abdomen; loops of intestine showed injection; the piece of liver was surrounded by omentum; the liver was spongy, friable, necrotic and gray brown
727	Fresh liver from another animal placed in the muscles of the abdominal wall; a piece being taken for culture first	70	27 hours	NPN fell from 53 mg to 26 mg per 100 cc of blood; Urea N fell from 28 mg to 12 mg per 100 cc of blood; NaCl fell from 554 mg to 376 mg per 100 cc of blood	Gram positive anaerobic bacillus cultured; broth culture negative	Gram positive anaerobic bacillus in liver substance; broth culture sterile	Odorless gas escaped when space was opened; space around liver lined with gray necrotic tissue; liver substance gray brown; spongy; necrotic; containing many gas bubbles
747	Fresh liver from another animal placed in the muscles of the abdominal wall; a culture being taken from this liver first	100	Killed after 40 days	None	No growth	Liver not cultured	Abscess developed around liver in the abdominal wall two days after operation; abscess broke through skin and animal survived; healing subsequently occurred

that anaerobic bacteria were obtained in cultures of the omentum from around the place where the liver substance had been. In two experiments, portions of fresh dog's liver that had been autoclaved as described were reinfected by infiltrating them with a culture of the anaerobic bacillus obtained from fresh liver. These reinfected fragments were placed in the abdominal cavities of two normal dogs. Both these animals died in twenty and thirty-six hours, respectively. The protocols of these experiments are summarized in table 3.

In the experiment just described, it is obvious that the autoclaving not only killed the infecting bacteria and their enzymes but also



destroyed the intracellular enzymes of the liver itself. Its absorption in the abdominal cavity must therefore be accomplished after hydrolysis brought about by invading phagocytic cells and their proteolytic ferments. To determine the influence of the autolytic enzymes of the liver in the production of toxic products, these enzymes were inactivated by heating portions of fresh liver to from 75 to 80 C for fifteen minutes. Such treatment does not destroy the bacteria present, and cultures revealed the same organisms after heating. These heated lobes of liver, when placed in the abdominal cavities of two normal dogs, caused

TABLE 3—*The Effect of Placing Autoclaved Liver (at 15 Pounds Pressure for 15 Minutes) in the Peritoneal Cavity*

Dog	Procedure	Length of Life	Bacteria of Fresh Liver	Bacteria of Autoclaved Liver	Bacteria of Liver at Autopsy	Observations at Autopsy
728	100 Gm. of autoclaved liver placed in the peritoneal cavity with aseptic precautions	Killed after 15 days	Gram-positive, anaerobic, spore-bearing bacillus	Sterile	Gram positive anaerobe	Autoclaved liver wrapped in omentum, about 25 cc of clear, straw colored fluid escaped when omentum was incised, only about half of liver had autolyzed in the fifteen days that animal had been kept
941	100 Gm. of autoclaved liver placed in the peritoneal cavity	Killed after 38 days	Gram-positive, anaerobic bacillus	Sterile	Gram-positive anaerobe in the omentum	Autoclaved liver entirely gone, fine mucus over omentum, dense adhesions between stomach and animal's own liver, abdomen somewhat distended by odorless gas during life subsequent to placing of liver in peritoneal cavity
908	100 Gm. of autoclaved liver in filtrate with a pure culture of organisms isolated from fresh dog's liver was placed in the peritoneal cavity	20 hours	Liver not cultured	Liver not cultured	Gram-positive, anaerobic bacillus	Autoclaved liver surrounded by loops of intestine, 30 cc of gray green pus around liver, liver mass gray green and friable, with little gas
938	100 Gm. of autoclaved liver in filtrate with a pure culture of organisms previously isolated from fresh dog's liver, was placed in the peritoneal cavity	36 hours	Liver not cultured	Liver not cultured	Gram positive, anaerobic bacillus	Autoclaved liver in left upper quadrant of abdomen, wrapped in omentum, liver substance gray brown with soft black areas through it and no gas

Note The nonprotein N, the urea N and the NaCl of the blood were within normal limits

toxemia and death in twenty-two and thirty-six hours, respectively. The protocols are given in table 4. Conditions here are apparently similar to those in the experiment in which the autoclaved liver was later reinfected by the isolated bacteria. It seems probable that this organism forms exceedingly poisonous substances when permitted to grow in dead liver, and that it is the absorption of these poisons from the peritoneal cavity that causes death under the conditions of these experiments.

The experiments now to be described indicate that actual aseptic in-vivo autolysis of liver is not fatal. Pups, near term, were removed

by Cesarean section, and the liver and entire alimentary tract were secured with careful aseptic precautions. All cultures of these tissues yielded no growth. The fresh fetal livers and also the entire abdominal viscera were placed in the peritoneal cavities of normal dogs without

TABLE 4—*The Effect of Placing Dog's Liver That Has Been Heated to from 75 to 80 C into the Peritoneal Cavity*

Dog	Procedure	Length of Life Hr	Effect on Nonprotein N, Urea N and NaCl in Blood	Bacteria of Fresh Liver	Bacteria of Heated Liver	Bacteria of Liver at Autopsy	Observations at Autopsy
746	100 Gm. of liver cultured, then heated to 75 C for 15 minutes, again cultured and then placed in the peritoneal cavity	22	None	Gram-positive anaerobic bacillus, broth cultures negative	Gram-positive, anaerobic, spore-bearing bacillus	Gram-positive anaerobic bacillus	Transplanted liver mass firm smooth and gray-brown pink on its surface no formation of gas
749	100 Gm. of liver cultured, then heated to 75 C for 15 minutes, again cultured, and then aseptically placed in the peritoneal cavity	36	NPN rose from 33 mg to 56 mg per 100 cc of blood urea N rose from 15 mg to 36 mg per 100 cc of blood NaCl fell from 552 mg to 425 mg per 100 cc of blood	Gram-positive anaerobic bacillus	Gram-positive anaerobic bacillus	Liver not cultured	Diffuse general peritonitis transplanted liver entirely necrotic mushy gray brown and containing much gas

TABLE 5—*The Effect of Placing Fetal Liver into the Peritoneal Cavity of the Dog*

Dog	Procedure	Length of Life	Effect on Nonprotein N, Urea N and NaCl of Blood	Bacteria of Fresh Liver	Bacteria of Fresh Liver	Observations at Autopsy
924	Entire liver secured aseptically from a cesarean section pup and placed into the peritoneal cavity	Killed after 26 days	None	Sterile	Nothing to culture	Peritoneum everywhere smooth and shiny no adhesions no trace of fetal tissue placed in abdomen
926	Entire abdominal viscera secured from a cesarean section pup and placed in the peritoneal cavity	Killed after 26 days	None	Sterile	Nothing to culture	Peritoneum everywhere smooth and shiny no adhesions no trace of fetal tissue placed in peritoneal cavity
620	A sterile fetal liver was infiltrated with a pure culture of anaerobic organisms which had previously been isolated from a healthy dog's liver; this infiltrated liver was placed in the peritoneal cavity	Killed after 26 days	None	Sterile	Gram positive anaerobic bacillus cultured from abscess wall and the pus	An abscess surrounded by omentum was adherent to the anterior abdominal wall; it contained about 20 cc of thick gray green pus; no liver tissue remained

ill effect. Examination made after twenty-six days showed no evidence of the transplanted tissues, all having been absorbed.

The toxemia associated with autolysis of the normally infected liver of dogs is so profound and death occurs so rapidly that there is little time for any marked changes to occur in the chemistry of the blood.

For the most part, the nonprotein nitrogen, urea nitrogen and chlorides remain within normal limits. In some cases, a fall in chlorides similar to that observed in certain cases of experimental peritonitis was found.

## COMMENT

The difficulties of getting sterile tissue for the study of autolysis have long been recognized. Most studies on autolysis *in vitro* have been made by the antiseptic rather than the aseptic method. The usual procedure has been to incubate the tissue between layers of toluol and chloroform as antiseptics.

Magnus-Levy<sup>5</sup> studied the aseptic autolysis of the livers of dogs and cattle. Agar cultures were made to check the sterility of these organs. Securing sterile livers was difficult. The chief organisms present were fermentative rather than putrefactive. In the livers that apparently proved sterile, he found a rapid production of organic acids and gases when the livers were incubated at 37 C.

Jackson<sup>6</sup> made similar studies on the "in vitro aseptic autolysis" of dog's liver. Agar cultures were made of the tissue to determine sterility. He made the statement that antiseptics such as chloroform and toluol markedly inhibited the rate of autolysis.

Wolbach and Saiki,<sup>7</sup> with extreme precautions against contaminations, cultured the livers of twenty-three dogs. Twenty-one of the twenty-three livers contained an organism which was difficult to grow on ordinary mediums, but which could be grown on a sterile extract of liver. It was a large, spore-bearing anaerobe which had the power of splitting glycogen and protein with marked formation of gas.

Jackson<sup>6</sup> noted that autolysis was extremely slow in the two sterile livers secured by Wolbach and Saiki.<sup>7</sup> At the end of forty-eight hours, the liver tissue was firm. There was no formation of gas. Lactic acid could not be detected by ordinary means. Jackson concluded that the changes which he and Magnus-Levy had previously seen were due to the action of this peculiar organism frequently present in normal dog's liver. The inhibition by antiseptics seemed to be an inhibition, not of autolysis, but of this organism.

There is considerable evidence that the tissues of normal, healthy animals may regularly contain bacteria. Reith<sup>8</sup> cultured the muscle

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5 Magnus-Levy, A. Ueber Saurebildung bei der Autolyse der Leber, *Beitr z chem Phys u Path* **2** 261, 1902.

6 Jackson, H. C. Rate of Aseptic Post-Mortem Autolysis, *J Exper Med* **11** 55, 1909, The Rate of Autolytic Reaction, *J M Research* **21** 281, 1909.

7 Wolbach, S. B. and Saiki, Tadasee. A New Anaerobic Spore-Bearing Bacterium Commonly Present in the Livers of Healthy Dogs, *J M Research* **21** 267, 1909.

8 Reith, A. F. Bacteria in the Muscular Tissues and Blood of Apparently Normal Animals, *J Bact* **12** 367 1926.

and blood of hogs, rabbits and guinea-pigs and obtained bacteria in a high percentage of his attempts. Bacteria were present in tissue secured from living animals, as well as in material secured from the packing houses. Anaerobic cultures were positive in a high percentage. Hauser<sup>9</sup> found bacteria in from 7 per cent to 43 per cent of cultures of the spleen, kidney, liver, heart and muscle. Bacteria were present in 14.8 per cent of all cultures of liver. He held that these were due to air contamination, and not to the presence of organisms in the tissue. Neisser<sup>10</sup> denied the presence of micro-organisms in normal tissues. Opitz<sup>11</sup> found the liver, spleen and mesenteric lymph glands free from bacteria, except in rare instances. Criticism might be directed at their work because the results of all cultures were recorded at the end of seventy-two hours. A longer time might have changed these results. Ford<sup>12</sup> cultured the livers and kidneys of dogs, cats, rabbits and guinea-pigs. From 75 per cent to 88 per cent of the cultures were positive. Cat fetal organs were sterile. He also showed that each animal had in the tissues its own distinctive kind of bacteria. A series of cultures of human liver, kidney and spleen were 100 per cent positive. Conradi,<sup>13</sup> with special precautions for sterilizing the surface of the tissue, found bacteria in the normal tissue of slaughter house animals, the positive cultures varying from 66 per cent in the case of cultures of liver to 9 per cent in the case of cultures of spleen. Bierotte and Machida<sup>14</sup> obtained similar results. Amako<sup>15</sup> maintained that the method of sterilizing the surface of the tissue used by both Conradi and Bierotte and Machida had been faulty. He found bacteria in the normal tissue as frequently as they, but believed it impossible to eliminate contaminants.

All these studies, except those of Reith, were done on the tissues of killed animals. Reith cultured the muscle and blood of living anesthetized animals. Berg, Zaw and Jobling<sup>16</sup> cultured, simultaneously, liver

9 Hauser, G. Mikro-organismen in lebende gewebe. Arch. f. Exper. Path. u. Pharmacol. **20** 162, 1886.

10 Neisser, Max. Ueber die Durchgangigkeit der Darmwand fur Bakterien. Ztschr. f. Hyg. u. Infektionskrankh. **22** 12, 1896.

11 Opitz, E. Beitrage zur Frage der Durchgangigkeit von Darm und Nieren fur Bakterien. Ztschr. f. Bakterien **29** 505, 1898.

12 Ford, W. W. Bacteriology of Healthy Organs. Trans. Am. Phys. **15** 389, 1900. Bacteriology of Normal Organs. J. Hyg. **1** 277, 1901.

13 Conradi, H. Ueber Keimgehalt Normaler Organe. Munchen med. Wchnschr. **56** 1318, 1909.

14 Bierotte, E. and Machida, S. Untersuchungen über Keimgehalt Normaler Organe, Munchen med. Wchnschr. **57** 636, 1910.

15 Amako, Tame. Ztschr. f. Hyg. u. Infektionskrankh. **66** 166, 1910.

16 Berg, B. N., Zaw, Z. D. and Jobling, I. W. Bactericidal Function of the Liver, Proc. Soc. Exper. Biol. & Med. **24** 433, 1927.

gallbladder bile and portal vein blood of living anesthetized dogs. The bile and blood were uniformly sterile, but the liver regularly contained anaerobic spore-bearing bacteria, apparently similar to or identical with the organism described by Wolbach and Saiki<sup>7</sup> and the one found in normal healthy dog's liver in our experiments.

The study of autolysis *in vivo* is made difficult by the regular presence of these organisms in the tissue. Such bacteria growing in tissue devoid of blood supply may well be the cause of the formation of toxic products which rapidly cause the death of the animal. Fetal liver, found sterile by culture, can be completely autolysed in the peritoneal cavity of an animal without harm.

#### CONCLUSIONS

1 The uncontaminated liver of a normal, healthy adult dog regularly contains a gram-positive anaerobic bacillus.

2 It is probable that the experimental so-called "in-vivo aseptic autolysis of the liver" is always accompanied by this infection and that this is the cause of death.

3 In-vivo aseptic autolysis of fetal liver, proved sterile by culture, does not produce any toxic effect.

# BILIRUBIN IN EFFUSIONS OF THE JOINTS

## METHOD OF ESTIMATION AND SIGNIFICANCE\*

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LOS ANGELES

The differential diagnosis between effusions of inflammatory and of traumatic origin is important from both a medical and an economic aspect, it guides therapeutic measures, and decides, in industrial and liability cases, the claim for compensation

The conclusion is based on the anamnesis, the objective signs of injury or infection and the character of the aspirated effusion The anamnesis can be misleading, minor injuries as well as infections are liable to be overlooked On the other hand, the history of an accident will be questioned unless supported by clinical observations, especially in cases that involve financial liability Abrasions, lacerations and other external symptoms are absent in a large number of traumatic effusions of the joints Roentgenograms are positive only in the presence of intra-articular fractures The character of the aspirated fluid is therefore the most valuable aid in these diagnostic problems

It is generally recognized that a hemorrhagic fluid indicates a traumatic etiology of the effusion While this is true in the majority of cases, there are exceptions which limit the value of the finding of blood Some diseases, such as sarcoma or hemophilia, can produce a hemarthrosis The puncture of a vessel during the aspiration can add blood to an exudate, an occurrence that is frequent and, therefore, an important source of error On the other hand, as blood is absorbed from the synovial cavity it will be missing if the aspiration is done some time after the injury

An estimation of the bilirubin content of the blood promised to clear up some of the doubtful points, and to make the differentiation more comprehensive

## BILIRUBIN FORMATION IN HEMORRHAGIC EFFUSIONS

After a hemorrhage into the joint has occurred, the red corpuscles break down The hemoglobin undergoes further changes and bilirubin is formed as an end-product The amount of bilirubin in an effusion depends on the quantity of red corpuscles from which it is derived, and the time necessary to form this end-product When bleeding is slight the amount of bilirubin is small even after all erythrocytes are broken down On the other hand a large hematoma contains in the first few

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days, almost intact red corpuscles and little bilirubin. On repeated aspirations, one will observe a decrease in the blood corpuscles and a proportional increase in the amount of bilirubin. Blood that is added to an exudate during aspiration cannot have an influence on the bilirubin content of an effusion. The color of the human blood serum, as well as of the joint fluids, depends mainly on the bilirubin.

#### METHODS OF IDENTIFICATION AND ESTIMATION OF BILIRUBIN

1 *Spectroscopic Examination* —The spectrophotometer is the most accurate and sensitive means of detecting bilirubin, but technical reasons prevent its clinical use.

2 *The van den Bergh Test* —The test is based on the fact that bilirubin combines with the diazonium salts, giving a red or violet color. Hijmas van den Bergh,<sup>1</sup> to whom physicians are indebted for most of their knowledge of this pigment in the blood serum, demonstrated two modifications of bilirubin.

The bilirubin that has passed the liver cells combines directly with the diazo reagent. Bilirubin that was not submitted to the action of the epithelium of the liver gives the reaction only indirectly. The serum or fluid is first mixed with double the amount of alcohol, and centrifugated. The albumin is precipitated, and the clear supernatant fluid is combined with the diazo reagent. The depth of the color developed is proportional to the amount of bilirubin present. It is matched in the colorimeter against a standard equal to 1 part of bilirubin in 200,000 parts of serum. The normal human blood serum contains between 0.3 and 0.6 of an unit.

3 *Icterus Index* —The yellow of human blood serum and effusions is caused chiefly by their content of bilirubin. A comparison of the depth of this color with a standard solution of potassium bichromate gives a quantitative estimation of the bilirubin. This method also originated with van den Bergh, but the practical application is due to the work of Meulengracht<sup>2</sup> and Bernheim.<sup>3</sup> The standard is equal to 15 units, normal serum has an index of 3 to 6 units. The advantage of this method is simplicity, a colored disk is available for the clinical type of colorimeters, also low priced special icterus index comparators are on the market.

The drawback to this method is that the yellow is not entirely due to bilirubin. Lutein and lipochromes frequently found in the blood serum also contain yellow coloring matter. When present in con-

1 Van den Bergh, Hijamas. *Der Gallenfarbstoff im Blute*. Leiden 1918.

2 Meulengracht E. *Deutsches Arch f klin Med* **137** 38 1921.

3 Bernheim Alice R. *Icterus Index. A Quantitative Estimation of Bilirubinemia*, J. A. M. A **82** 291 (Jan 26) 1924.

siderable quantity this will influence the icterus index. Recently Segall and Terry<sup>4</sup> pointed out this lack of specificity of the icterus index.

It is further clear that the icterus index cannot distinguish the two modifications of bilirubin brought out by the direct and indirect van den Bergh test. A high content of bilirubin of the blood will give a high icterus index equally when caused by an obstructive jaundice that gives both the direct and indirect van den Bergh reaction or by inflammatory, toxic and hemolytic jaundice that give a positive indirect van den Bergh reaction only. These objections should carry weight when the icterus index of the blood serum is employed as a test of the function of the liver.

My object, however, was to estimate the content of bilirubin formed locally in effusions of the joints. The possibility of detecting the source of a high bilirubin content of the blood with the van den Bergh test was immaterial. I used exclusively effusions from patients with normal bilirubin contents in the serum, only in these cases is the increase in the bilirubin proved to be formed locally from the hematoma. The lipochromes which interfere with accurate results in the serum, are mostly derived from food, they are transient and are not secreted into the joint fluid. With these objections eliminated, the icterus index appeared to combine simplicity and reasonable accuracy and was employed as the general method for my work.

As a preliminary to my study, I made a number of comparative examinations of joint fluids with the van den Bergh test and the icterus index. These fluids with high values of locally formed bilirubin up to 10 units (equal to thirty times the amount normally found in serum) gave without exception, a negative direct van den Bergh reaction. The values of the indirect van den Bergh reaction and the icterus index were in good agreement. This proves that the yellow of the fluid was due to bilirubin. The van den Bergh reaction and icterus index of nonhemorrhagic effusions (transudates and exudates) were equal or slightly lower than in the blood serum of the patient.

My routine procedure in the reported series was as follows. The aspirated effusions were centrifugated, the supernatant fluid was pipetted off from the sediment and the icterus index recorded. Only clear not hemolyzed fluids were used. Simultaneously a few cubic centimeters of blood was secured from the cubital vein of the patient and the icterus index of the serum controlled. Only cases in which the icterus index of the blood was normal were included in these studies. The icterus index was repeated with each subsequent aspiration.

<sup>4</sup> Segall G. and Terry M. C. The van den Bergh Test and the Icterus Index, California & Western Med. 28:3 (March) 1928.



## ANALYSIS OF MATERIAL

The basis of this investigation forms a series of fifty cases of joint fluid, forty-six (92 per cent) resulting from effusions of the knee and four (8 per cent) from the elbow joint. Forty-eight patients (96 per cent) alleged an accident, only two (4 per cent) did not make an injury responsible for the effusion. The traumatic etiology was clinically confirmed in thirty-two cases (64 per cent), and was not supported in fourteen (28 per cent) of the cases. Four cases (8 per cent) were regarded as doubtful. Of these fifty cases, the icterus index was estimated in thirty-five (70 per cent). The serum in the remaining fifteen cases (30 per cent) was either too cloudy or too hemolytic to estimate. This is apparently a high percentage, in which the test could not be applied, but thirteen of these cases were undoubtedly traumatic, including nine of fracture and disarrangements. Hence the differential diagnostic value of the test is not markedly reduced by the cases in which it could not be applied. Thirty-five effusions in which the icterus index was estimated are tabulated in three groups.

Table 1 gives the diagnosis, the interval between aspiration and the injury, the amount of fluid and icterus index of eighteen cases of joint effusions of traumatic origin in which objective observations were in agreement with the anamnesis. The analysis of this group reveals that the icterus index is higher than the icterus index of the blood serum, which was below 6 units, and varied in the fluids in the white range from 7.4 to 28 units.

With the exception of the first three cases, the icterus index in this group had a tendency to rise with the age of the effusion. Fluid aspirated from three patients in the first week of injury showed an icterus index of from 7.4 to 10, from five patients in the second week, an icterus index of from 10 to 18, from three patients between three and four weeks after injury, an icterus index of from 18 to 28 units. The latter figure is the highest icterus index in the series. From the twenty-eighth to the sixty-ninth day after injury a slight decline was noticed, the icterus index ranged from 16 to 21 units. This shows how slowly absorption from an injured joint takes place and emphasizes the therapeutic value of early aspiration.

The icterus index in effusions that were reaspirated increased from 5 to 10 units a week.

The time between the formation and the absorption or aspiration of the effusion was not the only factor responsible for the production of bilirubin in the joint cavity. The amount of hemorrhage was also important because blood is the material from which the bilirubin is formed. The quantity of fluid aspirated in this group varied from 4 to 90 cc. This explains the variation in the height of the icterus

index in effusions aspirated at nearly identical periods after injury. Some individual factors may also have an influence on formation of bilirubin in joint cavities.

The first three patients of this group had an icterus index of between 18 and 25 units although the effusion was aspirated on the first, second and third days after injury. This seems to be a contradiction to the above principles of local formation of bilirubin. The explanation is that all three patients had intra-articular fractures; hence venous blood from the bone-marrow had access to the joint cavity. Mann<sup>5</sup> and his co-workers proved, by animal experiments, that the bone-marrow is the

TABLE 1—*Traumatic Effusions*

Case	Diagnosis	Aspirated Ce	Days After Trauma	Icterus Index Units	Comment
1	Fracture of the internal condyle and spine of the tibia	50	1	18	
2	Fracture of the external condyle of the tibia	5	2	25	Incomplete aspiration of large effusion
3	Intra-articular avulsion	90	3	20	
4	Bursitis prepatellar	20	3	9.4	Reaspiration on seventh day; icterus index 16.6 less corpuscles
5	Bursitis olecrani	10	3	10	
6	Synovitis genu	50	4	7.4	Icterus index in the blood serum 4.1
7	Synovitis genu	25	8	15	
8	Synovitis genu	30	11	15.3	
9	Synovitis genu	10	13	10	
10	Bursitis prepatellar	25	14	18	Reaspiration on sixteenth day; icterus index 18
11	Synovitis genu	20	14	15	Few blood corpuscles
12	Bursitis suprapatellar	35	18	28	Varices around knee
13	Bursitis olecrani	5	21	18	
14	Bursitis olecrani	8	27	28	
15	Synovitis genu	12	33	18.2	
16	Bursitis prepatellar	20	33	16	Van den Bergh, indirect 3.8 units
17	Bursitis olecrani	8	35	21	Wassermann reaction four plus; blood and fluid van den Bergh indirect 5.7 units
18	Synovitis genu	40	69	19	Few blood cells

site of the largest production of bilirubin, and that venous blood from the bone-marrow had a high bilirubin content. The high icterus index in my cases of intra-articular fractures was therefore, due to bilirubin, not locally produced, but carried into the joint cavity with the venous blood from the bone-marrow. My observation is to my knowledge the first clinical confirmation of the splendid experimental work of Mann and his co-workers, and is of practical value for the diagnosis of intra-articular fractures as I pointed out elsewhere.<sup>6</sup>

5 Mann F C, Sheard Charles and Bollmann Jessie L. Evaluation of Relative Amounts of Bilirubin Formed in Liver, Spleen and Bone Marrow. *Am J Physiol* 78:384 (Oct.) 1926

6 Kling D H. Fat in Traumatic Effusions of the Knee Joint. *Am J Surg* 6:71 (Jan.) 1929

The bilirubin content in combination with the quantity of red corpuscles in the aspirated fluid can be used as an indication of the age of an effusion. In recent traumatic effusions, the icterus index and the volume of blood corpuscles have nearly the same values as in the circulating blood. If during aspiration blood is added to a nonhemorrhagic fluid, the amount of red cells will be slight and the icterus index normal. The more blood corpuscles that are broken down, the higher the icterus index rises. Hemorrhagic effusions will show in the first week an icterus index of about 10 units and a volume of 30 to 40 per cent of corpuscles in the centrifugated fluid. The cells diminish, and the icterus index rises to around 20 units in the second week.

Finally, after three or four weeks, only a small amount of red cells are left, while the icterus index is around 30 units. The volumes of corpuscles in blood and effusion can be easily compared with the hematocrit. When this instrument is not available, two graduated small test tubes of the same caliber are filled with equal amounts of effusion and oxalated blood from the patient. The samples are centrifugated at high speed for five minutes, and the volumes of cells in the two tubes are compared. Recently the erythrocytes of the aspirated fluid have been estimated directly in the blood counting chamber. According to the hemorrhagic content of the effusion one uses higher or lower dilution with Hayem's solution. Subsequently a red blood count is made, from which one abstracts the number of erythrocytes in the fluid. The difference then gives the amount of red cells broken down in the synovial cavity. If, for instance, 5,000,000 erythrocytes per cubic centimeter are found in the blood and 800,000 in the fluid, then 4,200,000 per cubic centimeter have been broken down. Either method is subject to error on account of the secretion of the synovial fluid, which will dilute the blood content and diminish the volume of red corpuscles as well as the number of erythrocytes. They are, therefore, of relative value, and should be used only for comparative study. The calculation of these factors permits a conclusion as to the age of the alleged injury, and a discrepancy with the observations of the history should be viewed with care.

In contrast with group 1, table 2 summarizes thirteen cases of inflammatory effusions. With the exception of two, these patients alleged an accident during work and claimed compensation. However, the clinical observations were negative for trauma, and the history was quite vague. Patient 1 claimed that another employee ran into him, patient 2 that he slipped but did not fall and patient 6 claimed that he was struck with the spine of a date leaf. They offered the clinical symptoms of inflammatory synovitis due to specific (gonorrheal syphilis or septic) or unspecific infection. The aspirations were made from five to forty-

three days after the onset of the effusion. The icterus index ran in the narrow range of from 3 to 5.2 units and was equal or slightly lower than in the blood serum. The fluids were turbid or limpid, and the Rivalta reaction was strongly positive. They did not contain blood. An increase of bilirubin was not observed in subsequent aspirations.

Finally, a group of four effusions of doubtful etiology is given in table 3. The history of the injury was quite definite, but was not supported by objective signs. The fluids were free from blood. The low

TABLE 2—*Inflammatory Effusions*

Case	Diagnosis	Aspirated Days After Onset	Icterus Index	Comment
1	Synovitis genu	3	4	Alleges collision with fellow employee
2	Bursitis suprapatellar	4	3.5	Struck knee lightly with wrench, kneels while working, reaspirated four times during 3 months, icterus index 2.5 to 4.3 units
3	Synovitis genu	5	4.7	Slipped but did not fall
4	Septic arthritis	8	5.2	Sepsis from infection of right hand
5	Bursitis olecrani	13	3.8	Cellulitis of elbow
6	Synovitis genu	27	4	Floor scraper, few red cells, housemaid's knee
7	Synovitis genu	43	5.3	Infection from spine of date leaf
8	Syphilitic synovitis	31	3.9	Wassermann of blood and fluid, four plus absorption after anti-syphilitic treatment
9	Synovitis genu	?	2.8	Housemaid's knee
10	Synovitis genu	?	4	
11	Synovitis genu	?	3.2	
12	Gonorrheal arthritis genu	?	4.7	Gonococci positive in urethra and culture of effusion, alleged trauma 'walking up stairs must have slipped
13	Tabetic atrophic genu	?	4	Optic atrophy, Wassermann reaction negative in blood and effusion

TABLE 3—*Effusions of Uncertain Etiology*

Case	Diagnosis	Aspirated Days After Onset	Icterus Index	Comment
1	Bursitis prepatellar	1	4	Transudate, blood negative, Rivalta reaction slightly positive
2	Bursitis prepatellar	8	4.6	Transudate, Rivalta reaction negative
3	Synovitis genu	43	3.5	Transudate, Rivalta reaction negative, specific gravity 1.013
4	Villous synovitis	330	4.2	Synovectomy

icterus index of from 4 to 4.6 units further indicated the absence of blood during the development of the effusion. While these factors contradict the history, there are some complications that do not permit elimination of traumatic etiology entirely.

The fluids in the first three cases showed the character of transudates, they were clear, pale, limpid, of low specific gravity, and reacted negatively or slightly positively to the Rivalta test. As a rule I found traumatic effusions to be hemorrhagic because of the rich blood supply of the synovium. It is doubtful whether a slight injury that does not rupture a vessel will produce a transudate in a joint. While one is

inclined to interpret such effusions on the basis of an irritation or inflammation, one must admit that there is not sufficient data available to exclude, entirely, the possibility of traumatic etiology of transudates

Case 4 reveals another problem wherein the icterus index at the time of aspiration does not give a hint as to the primary cause of the effusion

#### REPORT OF CASE

T P, a man, aged 25, fell and struck the right knee on the running board of an automobile. He developed pain gradually, consulting a physician fourteen days after the injury. He had a recurrent synovitis, and was seen in our hospital eleven months after the onset, when 20 cc of mucogelatinous fluid was aspirated. The sediment consisted of pus and endothelial cells. The Rivalta reaction was strongly positive, and the icterus index showed 42 units. At the operation, a villous synovitis was found and a synovectomy was performed. While the icterus index and the other characteristics of the fluid at the time of the operation were typical of inflammatory effusion, one must consider the possibility that the original effusion was hemorrhagic, and had a high bilirubin content, but was absorbed during the previous eleven months. There are no exact observations available on the time of absorption and on the character of the fluid in the recurrent effusions. A connection of the resulting inflammatory process with a primary injury, therefore, cannot be excluded.

#### COMMENT

This study of the icterus index brought forward the fundamental difference in the bilirubin contents of effusions. A group of eighteen cases of definite traumatic origin showed an icterus index higher than the blood serum and varying in a wide range of from 7 to 28 units. This is due to local formation of bilirubin, except in the cases of intra-articular fractures in which venous blood from the bone-marrow with a high bilirubin content is carried into the joint cavity. The amount of the locally formed bilirubin depends on the amount of hemorrhage and the interval between the formation and aspiration of the effusion. A gradual rise of the icterus index can be observed on subsequent aspirations, and a conclusion as to the age of an effusion can be deduced from the height of the icterus index and the amount of blood corpuscles in an aspirated fluid of traumatic origin. A second group of effusions shows an icterus index equal or slightly lower than the blood serum of the narrow range of from 3 to 5.2 units, which is not influenced by the time of the aspirations and does not rise on subsequent reaspirations. The majority of these effusions are evidently of inflammatory origin. Some dubious points in a small group of cases need further investigation eventually by other methods.

#### SUMMARY

The local formation of bilirubin raises the icterus index in traumatic, hemorrhagic effusions above the level of the blood serum. The icterus

index in inflammatory effusions on the other hand is equal or slightly lower than in blood serum

The locally formed bilirubin content depends on the amount of bleeding and on the time allowed for production. The icterus index therefore will increase and the blood corpuscles decrease in traumatic effusion. This permits one to draw a conclusion of the age of an effusion and to distinguish between a hemorrhage due to puncture during aspiration and an original hematoma. The icterus index in inflammatory effusions is not influenced by these factors nor does it vary on reaspirations.

In intra-articular fractures venous blood, rich in bilirubin, reaches the joint cavity from the bone-marrow, and raises the icterus index immediately, independent of any local formation of bilirubin. A high icterus index in a fluid aspirated immediately, or in the first days after the trauma is characteristic for intra-articular fractures.

The amount of blood corpuscles in an effusion can be estimated by the volume of the blood sediment or directly by the cell count and compared with the value in the circulating blood.

Several doubtful points require further investigation.

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# DISTRIBUTION OF THE BLOOD IN SHOCK

THE OXYGEN CONTENT OF THE VENOUS BLOOD FROM DIFFERENT  
LOCALITIES IN SHOCK PRODUCED BY HEMORRHAGE,  
BY HISTAMINE AND BY TRAUMA \*

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AND

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It is generally believed that there is a reduction in the volume of the circulating blood in all types of shock. In instances of shock without hemorrhage, the diminution of the blood volume is attributed to a passage of fluid from the blood into the tissues. The cause of the increased capillary permeability is as yet unknown, but most of the recent experimental work has seemed to support the view that it is the result of the presence of some toxic substance. Cannon believed that most of the harmful results of diminution in the blood volume are due to the reduction of the oxygen supply of the tissues. If the reduction in the oxygen supply of the tissues is an important factor in the pathogenesis of shock, then it would seem that information of value might be obtained from a study of the oxygen content of venous blood in various portions of the body. Such an investigation would offer an opportunity for a comparative study of the extent of the utilization of oxygen in different parts of the body in various types of shock.

## METHOD

Dogs were used in all experiments. Barbitol was employed as an anesthetic in practically all instances. The amount used was 0.3 Gm per kilogram of body weight. The barbitol was given in salt solution injected into the external jugular vein. The effects of barbitol alone were determined in many experiments at intervals varying from thirty minutes to sixteen and one-half hours after its administration. After the anesthetic had become effective, a cannula was placed in either the carotid or femoral artery in order to determine the arterial pressure. The level of the arterial pressure was used as an index of the degree of shock. The pulse rate and temperature were also determined.

The blood pressure was reduced to a low level, usually below 80 mm of mercury for the systolic pressure, by (1) hemorrhage, (2) the injection of histamine, (3) trauma to the intestines, (4) trauma to the cerebrum and (5) trauma to one of the legs. When shock was produced by hemorrhage alone, the amount to which the animal was bled usually varied from 3 to 35 per cent of its body weight. Histamine was given slowly intravenously until the blood pressure remained practically stationary at a low level. The usual amount of histamine that was required was 4 mg per kilogram of body weight. The cerebrum was traumatized by digital pressure until a fall in the blood pressure resulted,

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\* From the Department of Surgery, Vanderbilt University

after an opening had been made in the skull with a trephine and rongeur. This type of injury was usually accompanied by a moderate amount of hemorrhage. The intestinal trauma consisted of pinching the intestine and of making tension on the mesentery. It usually required at least an hour to cause a marked reduction in the blood pressure by this method. The leg was traumatized by striking it many times with a hammer in regions other than those occupied by the main artery and vein. This procedure was frequently supplemented by vigorous massage of the muscle. Usually, the femur and the skin were not broken.

Samples of blood were withdrawn for analysis from the right side of the heart, the renal vein, the portal vein, the external jugular vein, the femoral vein and the femoral artery. It was necessary to open the peritoneal cavity in order to obtain blood from the portal and renal veins. In most of the experiments in which one leg was traumatized, samples of blood were obtained from both femoral veins. The blood was withdrawn under oil and placed under oil in order to avoid contact with air. No stasis was produced in the collection of the samples, and if any difficulty whatever was encountered, the experiment was discarded. Blood from the right side of the heart was obtained by heart puncture, and all the other samples were obtained by inserting a small needle attached to a syringe into the lumen of the vessel. The blood gas analyses were performed with the Van Slyke-Neill manometric apparatus.

The order in which the samples of blood were obtained in all the experiments was as follows: (1) right heart, (2) portal vein, (3) femoral vein, (4) jugular vein, (5) renal vein and (6) femoral artery. Only a short time elapsed between the obtaining of the different samples and during this interval, in most experiments except the control ones, a quantity of blood equal to that which had been withdrawn was allowed to run into the jugular vein from a buret.

It was not considered necessary to perform control determinations in all the experiments in which shock was to be produced, since it was found in many experiments that the values for the oxygen content of the blood from the various vessels bore a surprisingly constant relationship to one another. In addition to this fact, it was desirable to produce the type of shock in which we were interested without having injured the veins by previous punctures.

## RESULTS

Ninety-seven series of determinations were performed on fifty-five dogs. The results of forty-five determinations on thirty-three dogs are recorded in the tables. Most of the earlier experiments are not reported because blood was obtained from three veins only and also because the sample of blood was not replaced by an equal quantity of blood. As was stated previously, all the experiments were discarded in which there was any difficulty in obtaining any of the samples.

Since the blood in the right side of the heart is a mixture of the venous blood from all parts of the body, the figure for this mixed venous blood is more or less used as a standard with which the others are compared.

*Control Determinations*.—The oxygen content of blood from the portal vein was usually approximately the same as that of blood from the right side of the heart, the average of all experiments showing a slightly lower content in blood from the portal vein. The oxygen content of blood of the femoral vein was usually definitely lower than that



of blood from the right side of the heart. This difference was usually greater the longer the animal had had barbital, and hence the longer it had been lying quietly on the table. Blood from the external jugular vein usually had a slightly higher oxygen content than did that from the right side of the heart. In all instances except two, in which they were approximately the same, the oxygen content of blood from the renal vein was higher than that of blood from the right side of the heart.

The average blood pressure in these experiments was 165 systolic and 101 diastolic, the average pulse rate 159 per minute and the average temperature 100.6 F. The accelerated pulse rate was caused by the barbital. The interval of time elapsing between the administration of barbital and the determinations varied from thirty minutes to sixteen and one-half hours. The figures for these experiments are recorded in table 1.

TABLE 1—Control Determinations

Ex- peri- ment	Oxygen Content, Volumes per Cent						Blood Pres- sure, mm Hg	Pulse Rate per min	Tem- per- ature, Fahr	Remarks
	Right Heart	Por- tal Vein	Fem- oral Vein	Ex- ternal Jugu- lar Vein	Renal Vein	Fem- oral Artery				
1	13.68	13.80	15.24	18.24	15.72	18.36	172/124	180	101.4	40 minutes after barbital
2	14.28	17.04	9.6	13.08	17.64	21.12	140/90	180	102.6	16½ hours after barbital
3	12.48	12.6	9.84	13.56	13.44		176/107	174	100.4	50 minutes after barbital
4	13.8	9.48	13.62	15.36	13.2	16.08	181/100	120	100.4	55 minutes after barbital
5	13.8	16.32	6.0	13.08	19.68		146/124	150	102	3½ hours after chloralose
6	17.04	13.8	18.0	17.64	18.96	20.4	160/92	160	102.6	55 minutes after barbital
Rep	16.8	12.3	11.76	17.4	19.8	20.88	156/106	175	100.6	4 hours after barbital
7	13.2	13.44	12.6	14.4	14.04	16.44	186/94	175	102	30 minutes after barbital
Rep	13.68	10.78	12.12	14.4	13.12	16.32	144/82	150	97.6	3 hours 25 minutes after barbital
Rep	11.4	12.96	6.48	10.2	14.28	16.8	132/78	160	97	4½ hours after barbital
8	5.28	6.0	5.76	7.08	5.52	7.98	186/98	156	101.4	40 minutes after barbital dog anemic
Rep	4.08	2.64	4.34	7.94	5.04		182/100	144	96.5	4 hours after barbital
9	14.4	14.76	7.92	14.76	17.04		192/104	160	102	2 hours 15 minutes after barbital
10	16.2	16.65	13.2	16.92	17.16		190/120	160	101.6	2 hours 25 minutes after barbital
Aver- age	12.88	12.32	10.68	13.86	14.54	17.14	165/101	159	100.6	

*Hemorrhage*—When the blood pressure had been reduced to a low level by bleeding the animal, the oxygen content of blood from the portal vein was usually approximately the same as that of blood from the right side of the heart. The oxygen content of blood from the femoral vein bore no constant relationship to that of blood from the right side of the heart. The average figure for all experiments was slightly lower than a similar figure for the mixed venous blood. The oxygen content of blood from the external jugular vein was also rather variable, the average figure being slightly higher than that for blood from the right side of the heart. The oxygen content of blood from the renal vein was higher in all instances than that of mixed venous blood.

The average blood pressure in these experiments was 58 systolic and 41 diastolic, the average pulse rate was 175 per minute and the average temperature was 101.4 F.

The point of interest in these experiments was that the average figures for the various determinations bore approximately the same relationship to one another as did the average figures for the control experiments. In both types of experiments the oxygen content was lowest in blood of the femoral vein next lowest in blood of the portal vein next in blood of the right side of the heart next in blood of the external jugular vein and highest in blood of the renal vein. This is shown in chart 1.

The figures for the experiments involving hemorrhage are given in table 2. The average highest and lowest figures are shown graphically in chart 2.

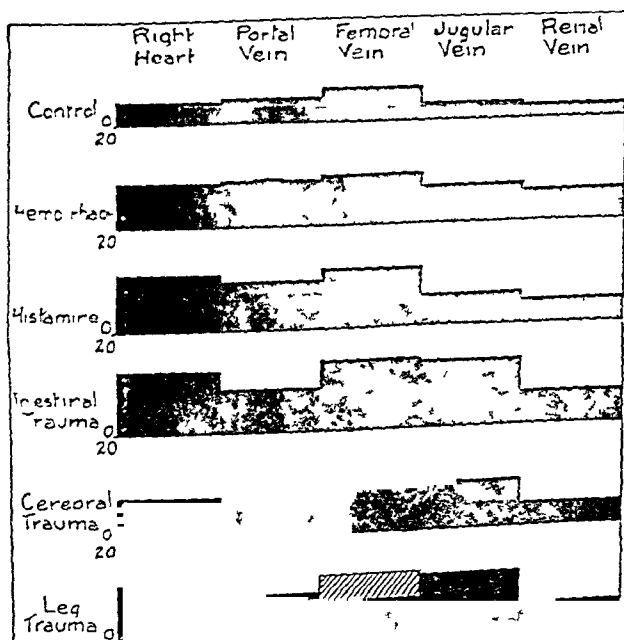


Chart 1—The average arteriovenous difference in oxygen content of blood expressed in volumes per cent, following hemorrhage, injection of histamine, intestinal trauma, cerebral trauma and leg trauma. The figures were arrived at by subtracting the oxygen content of the venous blood from that of the arterial blood in each experiment and obtaining the average for all experiments of a given type. Two values are charted for the femoral blood in the experiments involving trauma to the leg, the black block indicates the arteriovenous difference of the traumatized leg, and the lined one the difference of the opposite side. It is to be noted that the average values obtained during the control period and after hemorrhage, injection of histamine and cerebral trauma bear a rather constant relationship to one another.

*Histamine*—After the production of a low blood pressure by the injection of histamine the oxygen content of blood from the portal vein was usually slightly higher than that of blood from the right side of the heart, that of blood from the femoral vein was usually slightly lower

TABLE 2—*Effects of Hemorrhage*

Ex- peri- ment	Oxygen Content, Volumes per Cent						Blood Pres- sure, Mm Hg	Pulse Rate per Min	Tem- pera- ture, Fahr	Remarks
	Right Heart	Por- tal Vein	Fem- oral Vein	Ex- ternal Jugu- lar Vein	Renal Vein	Fem- oral Artery				
1	3.93	5.52	3.0	3.12	10.44	15.6	61/36	185	102.6	6 hours after barbitol no replacement bled to a total of 500 cc
2	4.08	6.36	5.88	5.88	8.52	13.56	35/25	190		No anesthetic ether for cannula, no replacement
3	5.28	2.40	1.56	6.60	6.48		42/30	200		4 hours after chloralose bled to about 350 cc no replacement
4	4.3	2.1	8.81	10.57	5.95		58/34	184	97.6	1 hour 20 minutes after barbitol, replacement
5	7.16	5.62	2.76	6.61	9.17	13.43	80/70	150	102.6	1 hour 35 minutes after barbitol, bled to a total of 540 cc, replacement
Rep	4.52	5.51	3.09	3.2	4.85	12.77	70/50	187	102.8	2 hours 30 minutes after barbitol, bled to a total of 640 cc replacement
Average	4.88	4.59	4.18	6.0	7.62	13.84	58/41	175	101.4	

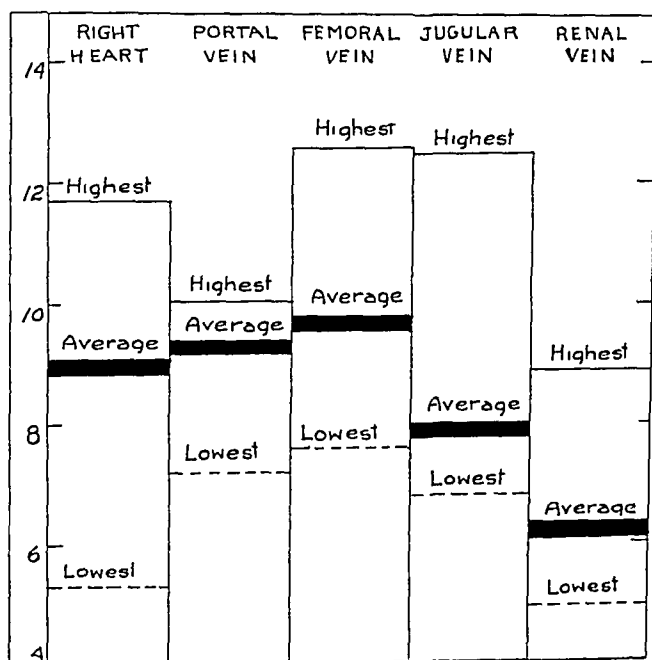


Chart 2—Arteriovenous difference in oxygen content of blood in shock following hemorrhage. In this and in subsequent charts, the heavy blocks marked "Average" indicate the average arteriovenous difference in oxygen content, expressed in volumes per cent, for all experiments of the type under consideration. The straight line marked "Highest" indicates the greatest arteriovenous difference in any one experiment, and the interrupted line marked "Lowest" indicates the smallest difference in any one experiment.

and that of blood from the external jugular and renal veins was always higher. The most striking difference on comparing these experiments with the control experiments and those with hemorrhage was that the

oxygen content of the blood from the external jugular vein was relatively higher after injection of histamine

The average blood pressure in these experiments was 52 systolic and 42 diastolic, the average pulse rate was 169 per minute and the average temperature 99.5 F

The results of these experiments are given in table 3 and chart 3

*Trauma to the Intestines*—After the production of a low blood pressure by trauma to the intestines, the oxygen content of blood from the portal vein was usually much higher than that of blood from the right side of the heart. The values for the oxygen of blood from both the femoral vein and the external jugular vein were usually slightly

TABLE 3—*Effects of Histamine*

Ex peri ment	Oxygen Content Volumes per Cent						Blood Pres sure Mm Hg	Pulse Rate per Min	Tem pera ture Fahr	Remarks
	Right Heart	Por tal Vein	Fem oral Vein	Exter nal Jugu lar Vein	Renal Vein	Fem oral Artery				
1	8.04	8.04	11.76	16.48	14.76	17.04	64/50	168	95.6	2 hours 15 minutes after barbitol histamine 40 mg replacement
Rep	4.92	7.08	4.56	9.0	12.12	15.84	36/25	144	95	2 hours 50 minutes after barbitol histamine 40 mg replacement
2	12.24	14.28	9.12	17.64	19.56	22.24	56/44	130	102.2	2 hours 10 minutes after barbitol histamine 30 mg replacement
Rep	7.2	10.92	6.48	11.88	16.44	20.76	42/35	170	102	3 hours after barbitol histamine 50 mg replacement
3	5.04	9.6	3.72	11.52	9.0		35/20	210	101	4½ hours after barbitol histamine 100 mg no replacement
4	12.36	11.76	9.96	14.52	16.2		100/80	180	101.5	3½ hours after barbitol histamine 20 mg no replacement
Rep	7.2	4.2	4.92	7.68	8.04		30/26	180	99.4	4½ hours after barbitol histamine 50 mg no replacement
Average	8.14	9.41	7.22	12.69	13.73	18.99	72/42	169	99.5	

lower than that of the oxygen of the mixed venous blood. The oxygen content of blood from the renal vein was always definitely higher than that of blood from the right side of the heart. The most striking observation in these experiments was the marked elevation of the oxygen content of blood from the portal vein as compared with that of the mixed venous blood.

The average blood pressure in these experiments was 50 systolic and 34 diastolic, the average pulse rate was 177 per minute and the average temperature 99.05 F.

The results of these experiments are to be seen in table 4 and chart 4.

*Trauma to the Cerebrum*—After a low blood pressure had been produced by trauma to the cerebrum, the oxygen content of blood from the portal vein, the femoral vein and the jugular vein respectively was

approximately the same as that of blood from the right side of the heart. With one exception, the oxygen content of blood from the renal vein was definitely higher than that of the mixed venous blood. The results in these experiments were similar to those in the control experiments and in the experiments with hemorrhage. The results are also similar to those found after the injection of histamine, except for the variation in the oxygen content of blood from the external jugular vein.

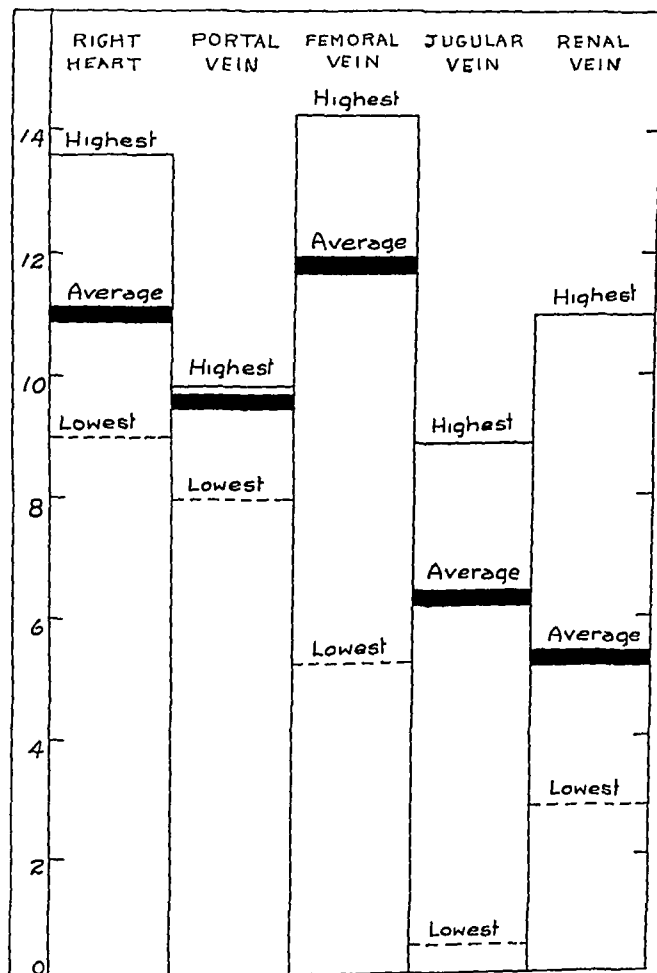


Chart 3—Arteriovenous difference in oxygen content of blood in shock following injection of histamine. Further explanation of the chart is given under chart 2.

The average blood pressure was 65 systolic and 50 diastolic, the average pulse rate was 163 and the average temperature was 100.4 F.

The results of these experiments are given in table 5, and the highest, lowest and average figures for arteriovenous difference are shown in chart 5.

TABLE 4—*Effects of Trauma to Intestines*

Ex- peri- ment	Oxygen Content, Volumes per Cent						Blood Pres- sure mm Hg	Pulse Rate per Min	Tem- pera- ture Fahr	Remarks
	Right Heart	Port- al Vein	Fem- oral Vein	Ex- ternal Jugu- lar Vein	Renal Vein	Fem- oral Artery				
1	6.96	9.24	4.2	6.12	14.16	22.56	65/54	144	102	2 hours 20 minutes after barbital replacement
Rep	6.84	9.0	4.44	4.92	12.6	17.28	54/44	100	102.2	4 hours 20 minutes after barbital replacement
2	6.12	14.25	6.00	6.48	10.32		40/30	210	97	5 hours after barbital replacement
3	10.2	15.36	7.56	8.4	17.4		50/25	180		No replacement 4 hours 50 minutes after bar- bital
4	5.28	5.64	3.12	3.12	7.44	17.76	42/20	190	95	5 hours after barbital no replacement
Aver- age	7.68	10.71	5.08	5.51	12.88	19.2	50/34	177	99.05	

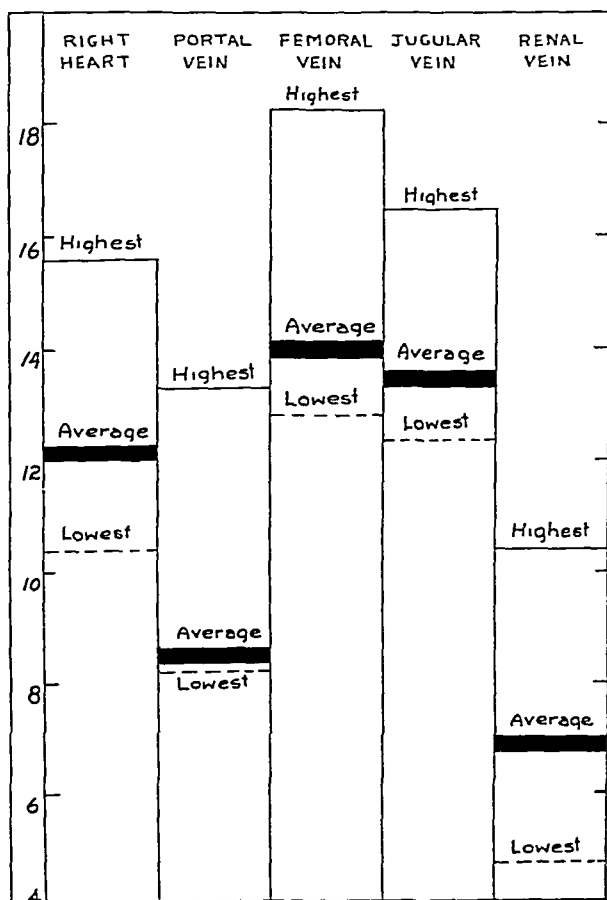


Chart 4—Arteriovenous difference in oxygen content of blood in shock following trauma to an intestine. Further explanation of the chart is given under chart 2.

TABLE 5—Effects of Trauma to Cerebrum

Ex- peri- ment	Oxygen Content, Volumes per Cent						Blood Pres- sure, Mm Hg	Pulse Rate per Min	Tem- per- ature, Fahr	Remarks
	Right Heart	Por- tal Vein	Fem- oral Vein	Ex- tern- al Jugu- lar Vein	Ren- al Vein	Fem- oral Artery				
1	6.8	6.84	4.8	6.0	11.76	14.22	60/50	200	104.2	3 hours 35 minutes after
Rep	5.16	4.8	5.28	5.52	9.60	14.28	45/38	206	104.2	barbital, replacement
2	8.52	7.8	6.84	6.48	15.0	17.4	60/40	144	102.2	4 hours 40 minutes after
3	6.36	8.0	6.24	9.0	5.76	13.2	90/70	180	94.8	barbital, replacement
4	9.6	9.84	8.88	11.4	11.28	16.2	72/52	135	99.4	4 hours after barbital
Rep	7.32	9.0	7.8	7.32	10.68	14.64	64/50	122	98	replacement
Aver- age	7.29	7.71	6.64	7.62	10.68	14.99	65/50	163	100.4	22 hours after barbital,
										replacement
										23 hours after barbital
										replacement

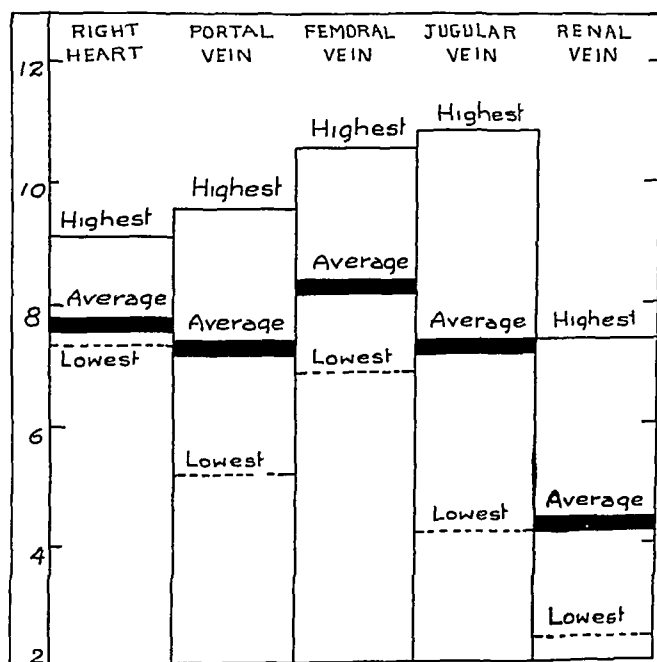


Chart 5—Arteriovenous difference in oxygen content of blood in shock following trauma to the cerebrum. Further explanation is given under chart 2.

*Trauma to One of the Posterior Extremities*—When a low blood pressure had been produced by trauma to one of the posterior extremities, the oxygen content of blood from the portal vein was usually about 2 per cent by volume higher than that of blood from the right side of the heart. The oxygen content of blood from the femoral vein of the nontraumatized leg was usually lower than that of the mixed venous blood while the content of blood from the traumatized side was

TABLE 6—Effects of Trauma to Leg

Oxygen Content Volumes per Cent												
Ex peri ment	Right Heart Vein	Por tal Vein	Femoral Vein		Ex ternal Jugu lar Vein	Renal Vein	Fem oral Artery	Blood Pres sure Mm Hg	Pulse Rate per Min	Tem pera ture Fahr		
			Non trau ma tized Side	Trau ma tized Side								
1	10.2	10.32	11.28		9.24	18.24	22.32	73/54	108	104.3	3	hours 45 minutes after barbital replacement
2	3.36	8.16	2.52		3.0	8.28	12.12	22/14	120	93.5	4	hours 10 minutes after barbital no replacement
3	2.16	5.88	3.0		4.2	6.60	12.0	45/40	142		5	hours 10 minutes after barbital replacement
4	4.56	6.36	2.4	11.88	3.36	9.48	18.24	65/58	140	99	4	hours after bar bital replacement
5	5.76	5.72	2.52	9.12	6.24	9.6	14.52	75/67	130	101.7	6	hours 25 minutes after barbital replacement
6	6.0	9.24	3.6	8.52	4.2	13.08	17.64	70/60	115	92.0	19	hours after bar bital replacement
Rep	4.56	6.84	3.72	6.96	2.52	9.96	15.96	55/45	126	91.6	21	hours after bar bital replacement
Aver age	5.23	7.0	4.15	9.12	4.68	10.53	16.11	55/48	129	97.01		

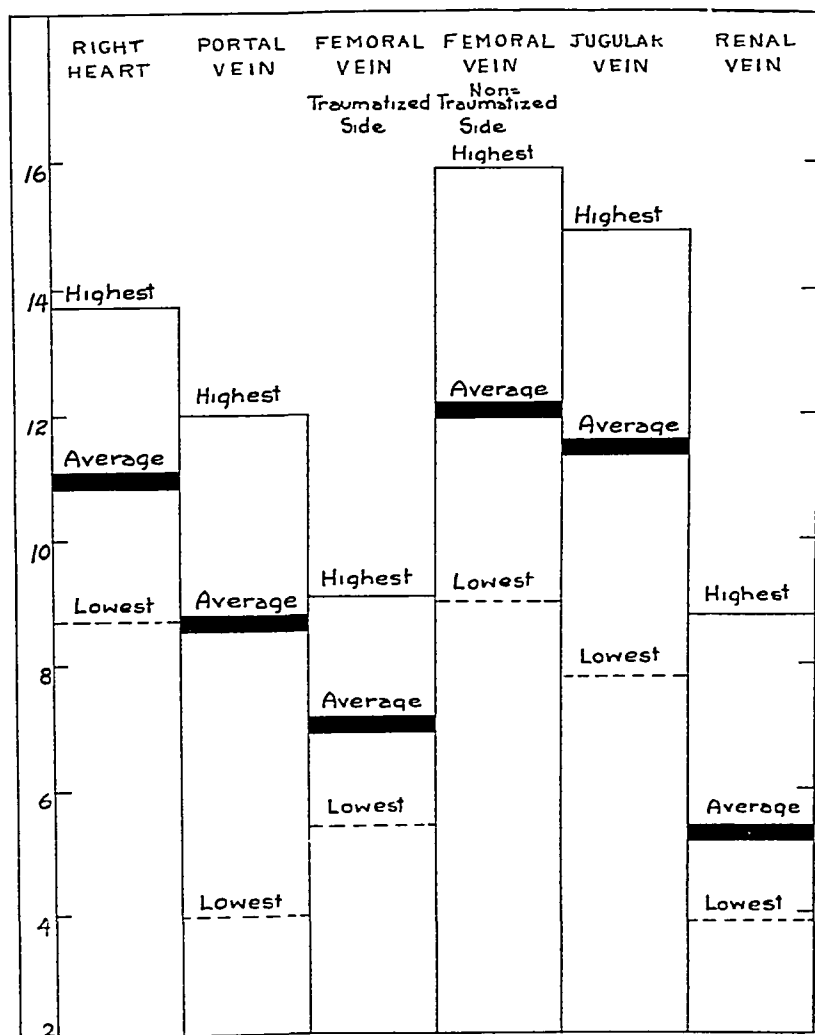


Chart 6—Arteriovenous difference in oxygen content of blood in shock following trauma to a leg. Further explanation is given under chart 2.



always considerably higher. The oxygen content of blood from the renal vein was always higher than that of the mixed venous blood, while the content of blood from the external jugular vein was usually about the same. The most striking point in these experiments was the high content of oxygen in blood from the femoral vein of the traumatized side.

The average blood pressure in these experiments was 58 systolic and 48 diastolic, the average pulse rate was 129 per minute and the average temperature was 97 F.

The results of these experiments are to be seen in table 6 and chart 6.

#### COMMENT

The veins from which the samples of blood were withdrawn were chosen with a definite point in view. The portal vein allowed us to obtain blood which was returning from the intestinal tract. It was desirable to employ a vein which collected blood from muscular tissue almost exclusively, and the femoral answered this purpose. It would have been much more desirable to have used the internal jugular vein rather than the external, because we were interested in obtaining blood which was returning from the brain. The internal jugular vein was too small to afford a sample of sufficient size for analysis. The external jugular vein was chosen after inability to use the internal had been demonstrated, because some of the blood from the brain of the dog returns to the heart by way of the former. This is probably small in proportion to the total amount of blood in the vein. The renal vein drains blood from a very essential organ and hence was chosen. Blood was not obtained from the coronary sinus of the heart because this would have necessitated the opening of the thorax. The veins leading from such organs as the suprarenal glands, the thyroid gland and the pancreas were too small to allow one to withdraw blood without the production of stasis.

The oxygen content of blood from the renal vein was higher in approximately all instances in all types of shock than that of blood from any of the other veins. The blood flow through the kidney is normally very great in proportion to its size, and the small arteriovenous difference in oxygen content indicates that the blood flow through the kidney in shock continues to be relatively large. Severe shock is associated with an acidosis, and it is important that the flow of blood through the kidney should remain elevated as much as possible in order to eliminate the acid.

In the experiments in which a low blood pressure was produced by the injection of histamine, the oxygen content of blood from the external jugular vein was unusually high. If this single determination is omitted from the consideration for the moment, it is to be noted that there is a striking similarity in the relationship between the values of the oxygen

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In the experiments in which a low blood pressure was maintained, the oxygen content of the jugular vein was unusually high. If this single factor is considered for the moment, it is to be striking similarity in the relationship between it

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In the experiments in which a low blood pressure was produced by the injection of histamine, the oxygen content of blood from the external jugular vein was unusually high. If this single determination is omitted from the consideration for the moment, it is to be noted that there is a striking similarity in the relationship between the values of the oxygen

content of blood from the various veins in the control experiments, and that between the values of the oxygen content of blood from these veins in shock following hemorrhage, the injection of histamine and brain trauma. This observation suggests that hemorrhage, histamine and brain trauma produce a fairly uniform diminution in the volume of the circulating blood in all parts of the body.

In the experiments involving trauma to the intestines, it is found, on comparison of the oxygen content of blood from the portal vein and that of blood from large areas of muscle with the oxygen content of blood from the right side of the heart that the portal content is unusually high and that of blood from the muscle low. In the experiments in which one of the legs was traumatized, the oxygen content of blood from the femoral vein of the injured extremity had a high content of oxygen while blood from the opposite femoral vein and that from the external jugular vein had a low content. The oxygen content of blood from the portal vein in these experiments was slightly higher than that of blood from the right side of the heart, but not strikingly so. In summary, it was found that blood from the traumatized area, whether it was the intestinal tract or an extremity, had an unusually high content of oxygen. These observations suggest that there was an accumulation of blood in the area that was traumatized and an unusual diminution in the amount of blood in other areas, with the exception of organs such as the kidney.

These experiments will have to be supplemented by others of a different nature before any final conclusions can be reached. The results at present indicate, but do not prove that the mechanism which operates after trauma to a large area of the body such as the intestinal tract or an extremity is different from that which operates following hemorrhage or the injection of histamine or trauma to the brain. It would seem that trauma to the intestinal tract or to an extremity produces its effect by a local accumulation of blood and not by an increase in capillary permeability in the general circulation with a loss of fluid into the tissues such as is attributed to histamine.

#### SUMMARY

- 1 The oxygen content of blood from (1) the right side of the heart, (2) the portal vein, (3) the femoral vein, (4) the external jugular vein, (5) the renal vein and (6) the femoral artery has been determined in dogs to which barbital had been given for varying intervals of time.

- 2 Similar studies were made after a low blood pressure had been produced by (1) hemorrhage, (2) the injection of histamine, (3) trauma to the intestinal tract, (4) trauma to the cerebrum and (5) trauma to one of the posterior extremities.

3 In the control experiments, the oxygen content of blood from the right side of the heart and that of blood from the portal vein were approximately the same, that of blood from the femoral vein was usually lower and that of blood from the external jugular vein slightly higher. The oxygen content of blood from the renal vein was usually definitely higher than that of the mixed venous blood.

4 Approximately the same relationship existed between the values of the oxygen content of blood from the various sites after a low blood pressure had been produced by hemorrhage, by histamine and by trauma to the brain.

5 The oxygen content of blood from the portal vein was much higher relatively after trauma to the intestines while that of blood from the extremities and head was low.

6 The oxygen content of blood from the femoral vein of a traumatized leg was high, while that of blood from the opposite extremity and head was low.

7 The oxygen content of blood from the renal vein was relatively high in all the experiments.

8 These observations suggest a local accumulation of blood at the site of trauma to a large area such as the intestinal tract or an extremity, and are evidence against the action of a histamine-like substance that produces a general bodily effect.

# PRIMARY INTRAMUSCULAR HEMANGIOMAS OF STRIATED MUSCLE \*

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Our object in this paper is to call attention to a surgical condition the origin of which is obscure and the diagnosis of which is seldom made except at operation

In 1908, one of us<sup>1</sup> (J S D) published a report of a study on primary hemangiomas of the muscle with a review of the literature up to that time and added six hitherto unreported cases to the 147 cases found in published reports. We wish to add to this number eleven new cases, and we have taken this opportunity of reviewing the literature of the past twenty years and of bringing the subject up to date. Since 1908 forty-eight cases have been added to the 153 gathered in the previous report, with which the eleven cases to be outlined make a total of 212.

In March 1843 Liston described the first case which he called an erectile tumor in the popliteal space, and this was found to be an angioma of the semimembranosus muscle. The earlier writers probably considered cavernous angiomas of the muscles as similar to true erectile tissue because the gross appearance is much alike and because under certain conditions angiomas also change in size. In case 9 of our series the angioma changed in size during the physical examination. The difference was clearly made by Rigaud when he stated that the variation in size of angiomas is a passive erectility due to mechanical pressure of the blood stream, while the variation in true erectile tissue is active erectility due to nervous control.

In 1894, Muscatello made a careful study of these tumors dividing them into four varieties according to their histologic structure. In 1905 Sutter, reporting a series of forty-six cases including a review of the literature, stated that the varieties described by Muscatello were variously combined. In 1908, one of us (J S D<sup>1</sup>) reported 153 cases, including six new cases. In 1913, Coll<sup>2</sup> made a resume, reporting 164 cases.

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\* From the Surgical Department of the Johns Hopkins University and Hospital

1 Davis, J S. Primary Haemangiomata of Muscle, Bull Johns Hopkins Hosp 19 74 (March) 1908

2 Coll, P. Das primare Angiom der Aquergestriekten Muskeln Inaug Diss, Zurich 1913

Mondor and Huet,<sup>3</sup> in 1923, reviewed these tumors, reporting 168 cases. In 1925, 201 cases were reported, but this list included some angiomas primary to tendon sheaths and some of the tongue of doubtful origin. In this series of 212 cases we have attempted to exclude all cases of doubtful origin.

Unfortunately, we were unable to secure two reports, one by M. Seifaty from South America and the other by D. M. Sugano from Japan, they might have added other cases to the list.

#### DEFINITION

Hemangioma of the muscle is a tumor of more or less extensive vascularity due to malformation and proliferation of the preexisting vessels of the muscle.

When using the term, angioma, in this paper, we mean hemangioma of the muscle as distinct from lymphangioma. Whether lymphangiomas ever originate in muscle is still a question, as up to the present no cases of pure lymphangiomas of voluntary muscle have been found. Nevertheless, it is stated by some authors that all angiomas of the muscle arise from lymphangiomas, and that the blood is secondary to lymph. Under this heading fall the so-called hematomylphangiomas which are described by Monzaido, Ritschl and Lucke.

The tumor may be a simple proliferation of the preexisting vessels in a certain district of the vascular network of the muscle, forming a simple angioma. The existence of a simple angioma is also questioned by some authors who believe that it may be a simple hypertrophy of the vessels without any neoplastic tendency.

It is probably best to look on simple angiomas as a stage in the growth of these tumors toward the cavernous type. In his study, Sutter found these types combined, indicating that there may be stages in the growth. Colli<sup>2</sup> stated that the cavernous type was the only one appearing in the muscles.

#### ETIOLOGY

Numerous theories have been advanced as to the etiology of these tumors. According to Virchow, the angioma has its base as a primary dilatation and proliferation of already existing vessels, the changes occurring by way of diseased processes of the vasa vasorum in a definite vascular area. The cavernous spaces gradually develop through a hyperplasia of the walls of the vessels and a gradual disappearance of the intermediary tissue, which atrophies, thus forming a union between individual cavities.

Rindfleisch and Rokitsanski assumed that angiomas arise from connective tissue tumors independent of the vascular system and form a

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<sup>3</sup> Mondor, H., and Huet, P. Angiomes musculaires, J. de chir. 21:423 (April) 1923.

connection with the vessels in a secondary way. Rokitanski at first ascribed carcinomatous qualities to tungus hematodes but later stated that they were benign.

Pilzer offered the following explanation. Through rupture of a vessel a hematoma was formed in the surrounding tissue which was not absorbed and which acted as an irritant to the neighboring connective tissue the cells of which then formed the so-called endothelial layer. He tried to explain the failure of absorption by a congenital disturbance of development in a definite area of tissue.

Honsell inclined toward the idea of vascular fibromas. Monzardo expressed the belief that increased vascular tension in the seat of the tumor was the cause. Riethus, Wardrop, Jorge,<sup>4</sup> Mondor and Huet,<sup>5</sup> Serfaty<sup>6</sup> and others were inclined to the theory that the tumors were congenital anomalies.

Sutter believed that angiomas are probably primarily congenital malformations in the vessels which may be noted only in later years and that obstruction to drainage due to proliferation of the coats of the vessel walls and damming of the flow, caused the formation of the venous and cavernous spaces.

We believe that these tumors originate in a congenital anomaly with trauma as a secondary factor causing their growth. The congenital anlage is always limited to a certain district of the vascular network. The size of these tumors varies so much that it is easy to conceive some so small that they are never disturbed by trauma and are carried through life unnoticed. This brings up the question of multiplicity and it is interesting to note that in the 212 cases collected there are only three cases reported (Lichtenauer, Reboul, Poucele).

The factor which causes the growth of these areas, probably trauma, may enter at any time. Some are already growing at birth, and others do not begin growth until some time later. In the case reported by Baumgartner<sup>6</sup> (11, table 1) the tumor was present from youth and did not grow rapidly until the patient was more than 60.

Trauma can be varied. The movements of the muscle itself can be irritant, stimulating the growth. Infections may cause an inflammatory reaction which in turn may stimulate the tumor growth. Guyot and Jeanneney<sup>7</sup> reported an angioma in the soleus and peroneus muscles after a mild attack of grip (77, table 1). The application of casts may cause

4 Jorge J. M. Sobre el angioma difuso de los musculos voluntarios, *Rev. Asoc. med. argent.* **23** 1448, 1915.

5 Serfaty M. Angioma mixamatoso del musculo biceps del brazo derecho. *Semana med.* **27** 888, 1920.

6 Baumgartner, H. Zur Kenntnis des Haemangioma cavernosum linguae, *Schweiz. med. Wchnschr.* **55** 1030, 1925.

7 Guyot, E., and Jeanneney, A. Angiome musculaire primitif de la brache externe de la jambe, *pathogenie*. *J. de med. de Bordeaux* **94** 564 (Sept. 10) 1922.



the growth to begin, as in Furnau's<sup>8</sup> case (63, table 1) Birth trauma, blows, falls, etc., may also be causative agents

#### SYMPTOMS

*Functional or Subjective*—Pain can probably be considered the chief symptom, because it is the one that usually causes the patient to seek treatment In our summary of cases we find that pain was reported in 100 of the 123 cases in which there is a definite note on the presence or absence of pain Benard and Lamy<sup>9</sup> believed that pain was a diagnostic aid and thought that the word *doloureux* should be added to the name of these tumors We know, however, that pain can be entirely absent even when the tumor has been present for a long period of time, as in the cases of Gold<sup>10</sup> (69, table 1) and of Gorse<sup>11</sup> (72, table 1) in both of which there was no pain after sixteen years In our new series of eleven cases, nine gave a history of pain, and in the six cases previously reported by one of us (J S D) five had pain

Pain is caused either by pressure of the tumor on a nerve trunk or by involvement of a nerve in the tumor itself The situation of the tumor with regard to the sensory nerves determines the appearance and the intensity of the pain The angiomas of the long narrow muscles find it difficult to spread without exerting pressure on some nerve branch, while the wide flat muscles of the neck or trunk offer a greater field of expansion before pressure on sensory nerves occurs Eleven of the twenty-three reporting the absence of pain in the 212 cases occurred in the muscles of the head and trunk, although the muscles of the extremities were involved in almost twice as many cases

Mechanical functioning of the musculature and the posture of the patient also play a rôle in causing pain There may be no pain when a muscle is at rest, but when the muscle thickens in contracture, there is pressure on a nerve, as in the cases reported by Mondor and Huet<sup>7</sup> (119, table 1) and by Diedoff<sup>12</sup> (51, table 1) Also, there may be no pain when a patient is lying down, however, when the patient is up or walking the pain may appear, as in case 4 The application of a cast may cause sufficient pressure to bring pain, as a case reported by Furnau<sup>8</sup> (63, table 1) and case 7 show

8 Furnau, F Beitrag zur Klinik der primären Muskelangiome, Arch f klin Chir **131** 495 (Sept 23) 1924

9 Benard, E, and Lamy, J Angiomes profonds douloureux des membres, Presse med **17** 907 (Dec) 1909

10 Gold, E Zur Klinik und Histologie der Hämangiome der Skelettmuskulatur, Deutsche Ztschr f Chir **181** 74 (Aug) 1923

11 Gorse, P Des angiomes intra-musculaires, Rev de chir **46** 83 (Juli) 1912

12 Diedoff, V Rare Case of Angioma in the Flexor Carpi Radialis, Khirurgiya Mosk **26** 556 1909

The inclusion of nerves in the tumor caused pain in some cases. In these cases Benard and Lamy<sup>9</sup> demonstrated nerve fibers in the periphery of the tumors, Kirrnisson<sup>12</sup> found a nerve encased in the tumor. The nerve fibers, however, are resistant and microscopically were normal in all the cases, even when the muscle tissue showed atrophy. Removal of the tumor caused the pain to disappear, demonstrating that there was no lesion in the nerve itself but that inclusion or pressure caused the disturbance.

Pain may be localized over the tumor or it may be diffuse, it also varies in duration and intensity. Kirrnisson<sup>13</sup> (93, table 1) reported that in his case the pain was localized over the tumor and was so severe that the mass could not be palpated except under an anesthetic. Mondor and Huet<sup>2</sup> (117, table 1) reported a case in which the pain was localized over a point in the lower part of the abdomen; they performed an operation for pelvic inflammatory disease through a midline incision. They found that there was no lesion in the pelvis, so a second incision was made over the painful area and an angioma was found in the rectus muscle. Guyot and Jeanneney<sup>7</sup> (77, table 1) reported a case in which the whole leg was painful. In a number of cases the pain was spontaneous, persisted for a time and then disappeared. In others it appeared as a constant severe pain and then disappeared for a time, only to reappear. In a case reported by Guyot and Jeanneney pain appeared after an attack of grip. Phleboliths may cause pain, as in the case reported by Wakeley<sup>14</sup> (197, table 1) in which painful nodules were palpated. Then again pain may be entirely absent even when a nerve is found in the tumor, as in the case reported by de Busscher<sup>15</sup> (30, table 1).

According to the consensus of opinion the chief characteristic of pain in these tumors, when it is present, is that it is spontaneous in many cases. Hemangiomas cause pain passively, that is through mechanical action, if that action does not happen to affect some adjacent nerve, there will be no pain.

Besides pain angiomas may cause numbness or formication, heating and burning, or pricking. Wakeley<sup>14</sup> (197, table 1) reported itching more severe at night. Magnon (106, table 1) reported numbness followed by heat and burning.

The third subjective symptom is the impairment of function. In forty-seven cases there was some impairment of function, ranging from a slight limitation of motion to deformities of the extremities with

13 Kirrnisson M E Des angiomes profonds douloureux des membres, Bull Acad de med, Paris **71** 849 (June) 1914

14 Wakeley, C P Calcification in Angiomata, Arch Radiol & Electroth **25** 363 (May) 1921

15 De Busscher L A propos d'un cas d'angiome volumineux du bras, Bull Soc de med de Gand **76** 45 1909

an almost complete loss of function. Causes for the impairment of function are pain, the growth of the tumor in the muscle and the size of the tumor mass which prevents a group of muscles from functioning normally.

Case 4 illustrates the loss of function because of pain. The patient was unable to perform her work because of pain and tingling in the fingers. One can readily see from the preceding paragraphs that pain can cause functional impairment.

The growth of the tumor in a muscle causes destruction of the muscle tissue and replacement by tumor tissue and fat. The contractile elements of a muscle are destroyed and it loses its function, with the resulting loss of function of that part of the body. In case 2 the tumor had invaded the muscles of the calf, causing shortening and a marked deformity of the leg with loss of function. In the case reported by Jorge<sup>4</sup> (85, table 1) there was a gradual loss of function as the tumor involved the muscles of the forearm. In our series, thirty-seven cases were reported in which there was some impairment of function, and all of these cases occurred in the upper or lower extremities, in other words, thirty-seven of 138 patients had functional impairments. These tumors assume a malignant aspect when one considers that they inevitably terminate in the loss of function or in the sacrifice of an extremity if proper treatment is not carried out at an early stage.

The size of the tumor can also impede the function of adjacent muscles. In the case of Fritzsche (61, table 1), the mass was the size of a small pumpkin, situated in the semimembranosus and semitendinosus muscles and impaired the function, causing a limp. Sutter (180, table 1) reported a tumor the size of a goose egg in the supinator longus muscle which interfered with the motion of the elbow. In the case reported by Honsell (82, table 1) the tumor was the size of the head of a fetus and caused contracture of the leg.

Interference with function always comes late, and usually so much damage has been done that operative measures merely prevent further deformity and further impairment of use.

*Physical or Objective Symptoms*—The objective symptoms are those which lead to the diagnosis of muscular angioma. Swelling is really the only objective symptom. The amount of swelling varies greatly. There may be no palpable mass, due to the situation of the tumor in the deep musculature, or it may be so small that it is seen only when it is cut down on. The size ranges from that of a nut to that of a small pumpkin. The tumor is not tender in itself, and if tenderness or pain is present, it is due to the proximity to sensory nerves, as was previously mentioned. Occasionally, the tumor is found at autopsy (37, table 1), no symptoms having been complained of during life. Sometimes the growth is discovered during an operation for some other condition as in

case 38 table 1 (Davis) in which the tumor was found in a child during an operation for varicose veins

It is well to repeat the suggestion made by one of us (J S D<sup>1</sup>) that a varicose condition of veins of leg in children can be caused by an angioma of the muscle and the tumor itself not be discoverable by swelling or any other symptoms, and only demonstrable by operation "

#### DIAGNOSIS

The diagnosis of these tumors is difficult because of the indefiniteness of the symptoms. One should always take into account the fact that an angioma originating in a muscle varies greatly in size and that it can be situated in a deep muscle as well as in a superficial one—all of which makes the symptoms vary

The diagnosis, until recently, was seldom made before operation, the comparative rarity and the depth of tumor being the principal reasons for the difficulty. Now it is recognized more often than formerly. In the 212 cases collected, only eighteen correct diagnoses were made before operation. The tumor can appear in any voluntary muscle. Examination therefore, will reveal a tumor of distinct size which, when it is visible will become more prominent by contraction of the muscle in which it is situated. Case 5 illustrates this point. At this same examination nevus or any other manifestations of the skin will be discovered. Nevus can accompany angiomas of the muscle, but their presence is merely accidental. The skin over the tumor is usually loose and freely movable; however, it may be tense and shiny due to stretching over a rapidly growing tumor. It can also be bluish, due to the closeness of a tumor to the surface or to the invasion by the growth (Zampa,<sup>16</sup> 201, table 1). The vessels in the skin may be dilated. This dilation may range from a few enlarged venules to varicose veins. In the later case, one must be cautious in making the diagnosis since the skin of the subcutaneous tissue might just as well be the region of origin of the neoformation. In a case reported by Kolaczek (98, table 1) and in other observations of his reported in the literature, it was a matter of diffuse angioma of rapid growth, in which the skin showed intense, strandlike enlargements of the veins of the skin, which he interpreted as a compensating process for the compression of deeper veins by the tumor. In this case the veins reached the point of varices, while in the case reported by Coll<sup>2</sup> (33, table 1) there was no more than an enlarged network of veins visible through the skin. In other cases, the skin will be entirely normal.

Palpation again offers difficulties. Occasionally, there is pulsation in the early stage, as in Liston's case (103, table 1), Matsuoka (130,

<sup>16</sup> Zampa G. Emangioma cavernoso diffuso dei muscoli striati, Polichinico (Sect Surg) 32 40 (Jan 15) 1925

table 1, quoted by Nagatomi) reported a case of pulsation in the later stage. This pulsation may possibly be transmitted from a neighboring artery. There may be soufflé also, but these are uncommon phenomena in angiomas of the muscles. Palpation shows the tumor to be of varying consistency, generally soft, at times with nuclei or more consistent portions, which may be extremely hard. Maigaiucci (110, table 1) reported a case with an ossified center. Wakeley<sup>14</sup> (198, table 1) reported movable hard areas in a tumor which turned out to be phleboliths. The consistency of the tumor also changes with the contractions of the muscle. Determining the nature of the surface of tumors deeply located is not always an easy matter. In the reported cases the number having a smooth regular surface is equal to that of tumors of the opposite description. In most cases there is no distinct boundary, even the circumscribed angiomas usually show a gradual transition into the surrounding tissues. The tumor may be movable laterally when the muscle is at rest. It may be smooth, or there may be lobulations. Often the tumor is reducible but usually only partially, making it impossible to determine whether it is circumscribed or diffuse with various lobulations and with distinct limits. Magon's case (106, table 1) was completely reducible, Davis' case (40, table 1) was partially reducible, and Nagatomi's case (129, table 1) was not reducible. Ordinarily, these tumors cannot be completely reduced. The size of the tumor may also be reduced by raising the extremity on which it is situated or by obstructing the circulation of the segment. In the case reported by Strauch (175, table 1) a bandage was placed tightly about the neck causing the tumor to swell appreciably, several hours after the removal of the pressure it returned to its former size.

Compressibility has long been considered a valuable diagnostic point. It is not always present and when found cannot be absolutely depended on. To every eighteen patients showing this symptom there were twenty-three who stated expressly that it was absent. It is found chiefly in those angiomas of the muscles the liquid content of which can find its way into the veins. Fluctuation is occasionally found, but it is of no diagnostic value and is usually incorrectly interpreted. A characteristic symptom, helpful in diagnosis, is the presence of phleboliths. Wakeley made the diagnosis from an x-ray picture showing phleboliths. They are formed by calcification of organized thrombi and may be present at any age. They occur in the cavernous spaces as well as in the veins. Sometimes, if there is not too much connective tissue, these concretions are palpable. Many are so small that they are detected only by roentgen examination. Care must be taken to observe closely the shape of the shadows since only circular or oval shadows ranging from the size of a millet seed to that of a pea are characteristic. In Mahan's case (107, table 1) the shadow was so close to the bone that the diag-

nosis of tumor of the bone was made. In the thirty-three cases in which phleboliths were found in the tumor sixteen were found by roentgen examination and seventeen were discovered in the examination of the growth after removal. Deformity and loss of function due to muscular angiomas have already been discussed and these factors should always be borne in mind when the diagnosis is being considered in obscure cases. Exploratory puncture is used frequently as a means of diagnosis. It would seem logical to diagnose a neoformation as an angioma when a puncture yields normal blood and the tumor regains its original size in a short time. Some authors say that cavernous angiomas have been observed to increase in size at puberty. Another symptom which may aid in the diagnosis is excessive growth of the entire affected limb occasionally amounting to actual hypertrophy.

#### DIFFERENTIAL DIAGNOSIS

The following neotormations and diseases must be taken into consideration and differentiated from hemangiomas: lipoma, sarcoma, fibroma, hematoma, primary carcinoma of the muscle, dermoid cyst, hemangiomatous elephantiasis, syphiloma, chronic myositis, tuberculous myositis, myositis ossificans, hydatid cysts, hernia of the muscle and hernia of the lung.

Angioma of the muscle is most frequently diagnosed lipoma because of its soft lobulated structure, slow growth and the frequent lack of pain both spontaneously and on pressure. Careful examination will usually determine whether or not the growth is in the muscle, which fact will eliminate all lipomas excepting those primary to muscle, which are rare. Primary sarcoma of the muscle is exceedingly rare also; however the intermuscular sarcoma arising in the connective tissue between the muscle bundles must be considered. Exploratory incision will reveal the characteristic pathologic changes and the diagnosis can be made. Fibromas of the muscle have well defined borders, grow rapidly and are hard, neurofibromas are similar. In the collected cases, the condition was diagnosed fibroma or neurofibroma in nine, depending on the presence or absence of pain. Dermoid cysts are never found in the muscle of the extremities. Hydatid cysts will yield a clear yellow fluid and the characteristic hooklets can often be found microscopically. Syphiloma and tubercular myositis can usually be excluded by careful physical examination and laboratory tests. Syphiloma will clear up under antisiphilitic treatment. In tuberculous myositis an exploratory puncture will show thin serous fluid with caseous detritus. The condition in twelve cases was diagnosed as cold abscesses or tuberculosis in the series of cases collected. Primary carcinoma of the muscle has never, to our knowledge, been found and metastases can be eliminated by the absence of a primary growth. Chronic myositis and myositis

ossificans should offer no difficulties. In chronic myositis the swelling is extremely hard with a history of long continued pressure or trauma. In myositis ossificans there is bone formation, and the x-ray picture will establish the diagnosis. Hematoma can be eliminated by exploratory puncture, since it will yield dark blood if aspirated early, and serum if aspirated later, but never normal blood, and it will not return to its original size after it is once aspirated. There is also a history of recent injury. Hernia of the muscle changes size with the contraction or relaxation of the muscle, and a vent can usually be felt in the fascia. Hernia of the lung is rare and, of course, is found only on the wall of the chest. Ordinarily, it can easily be reduced, and the x-ray picture will establish the diagnosis.

Sometimes it is necessary, even after excision of small atypical angiomas of the muscle, to examine the growth microscopically before a final diagnosis can be made.

#### PATHOLOGIC CHANGES

Angiomas are considered benign tumors, although they have some characteristics which indicate a malignant tendency. They are always progressing. They infiltrate the muscle, which is the seat of origin, then extend to neighboring muscles, and soon penetrate the aponeurosis and other tissues until they reach the bones, which they may also invade. Their growth is not by expansion, as in the majority of benign tumors, but by infiltration. An angioma does not force back the tissues which surround it but infiltrates the adjacent tissue by small endothelial germs, which later give rise to the formation of capillaries. The interstitial connective tissue is invaded by endothelial cells forming capillaries, which destroy the muscle and give place to the fenestrated tissue which characterizes angioma of the muscle. The development is produced not by monocentric but by multicentric proliferation. From the periphery the angioma increases and radiates in different directions. The invasion is by continuity, a characteristic of malignant tumors. It is a question whether metastases occur. The appearance of metastatic formations, however, which have been cited by Konjetzny,<sup>17</sup> Walis, Billroth and others, is so extremely rare that the question arises whether they are angiomatous metastases or angiomatous tumors of another type.

The evolution of these angiomas *in situ* is serious, for the transformations and degenerations which other angiomas undergo and which interfere with their invasion are not observed in muscular angiomas.

Muscular angiomas sometimes cause thrombosis of the vessels (Vianney, 193, table 1) and cause profuse hemorrhages from the tumor, but if no communication exists with a large vessel, the flow of blood is slow, like the usual circulation in angiomas in general.

<sup>17</sup> Konjetzny, G. E. Zur Pathologie der Angiome, *Munchen med. Wchnschr.* 59: 241, 1912.

Some authors have described angiomas which have undergone malignant degeneration and others have reported cases of angiomas which have undergone suppuration after an intercurrent malady.

The classification as previously given by one of us (J S D<sup>1</sup>) is probably as satisfactory as any and follows

Simple or Telangiectatic Cavernous	Capillary Venous Arterial	Rare  More frequent	Circumscribed or Diffuse	Rare  Common
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Often, however, all the divisions of simple angiomas together with the cavernous type are found in the same tumor in different areas. The existence of the simple angioma is also questioned by some authors, who believe that simple angioma is only a stage in the development of cavernous angiomas.

We shall confine ourselves to the cavernous type.

The gross specimen looks much like a muscle containing varicose veins. The thin-walled cavernous spaces appear bluish as they protrude between the muscle fibers. The mass is more or less compressible. On section the tissue is red or reddish brown and gives the impression of a sponge filled with blood. The density depends on the amount of fibrous connective tissue. If the connective tissue is dense, then it will have the appearance of a fibrous tumor. If the connective tissue is loose, the blood filled spaces will be prominent and will give the appearance of a mass of varicose veins which have been cut across. Sometimes the vessels will stand out on the cut surface like small stems, the connective tissue having retracted. The muscle fibers may be unchanged or appear in different stages of degeneration. There may be areas of fat. There is an increase in the intermuscular fibrous tissue. The tendons and nerve trunks are rarely affected, and the large arteries are usually normal. Microscopically, cavernous angiomas are composed almost exclusively of blood filled lacunae limited by connective tissue septums which are often incomplete. In some of the lacunae the blood coagulates, forming clumps of fibrin which at times seems adherent to the wall, and at other times almost completely separated, being connected to the endothelial wall by a pedicle of fibrin. In these fibrinous masses neoformations appear which terminate in the formation of capillaries which distribute them in various directions. In some of the lacunae many red cells and a few white cells are seen. In others the number of white cells increases considerably, so that some authors have considered these spaces as lymph spaces.

In some angiomas there are deposits of calcareous salts which are surrounded by periodic desquamation of endothelium, producing concretions with concentric cellular layers.



TABLE 1—Table of 212 Cases

Author	Reference	Color	Age	Sex	Trauma	Duration of Tumor	Location and Size	Therapy and Result	Type, Symptoms, Comment
1 Agnew	Cited by Davis <sup>1</sup>	White	?	F	?	Congenital	Abdominal muscles	Excision, recovery	Cavernous angioma, pains, fluctuation, diagnosed cystic angelioma
2 Alessandri	Cited by Davis <sup>1</sup>	White	29	F	?	4 years, rapid increase in two months	Trapezius	Excision, recovery	
3 Miller	Cited by Davis <sup>1</sup>	White	?	?	?	?	Pectoralis major	?	Arterial circumscribed angioma, pains
4 Anzofotti	Cited by Davis <sup>1</sup>	White	29	M	?	3 years	Orbicularis palpebrae	Excision, recovery	
5 Autray	Cited by Davis <sup>1</sup>	White	20	F	?	2 years	Vastus internus	Excision, recovery	Capillary angioma, pains, diagnosed arthritis
6 Bland Sutton	Brit. M. J. 2, 1918	White	23	M	None	Congenital	Muscles of hand	Amputation, recovery	Capillary angioma, pains, diagnosed cavernous angioma, dilated vessels in skin, buzzing, pain six months, no phleboliths
7 Blijrd	Cited by Davis <sup>1</sup>	White	12	M	?	Over a year	Gluteus medius	Excision, recovery	Circumscribed cavernous angioma, diagnosis, neuroma fulsum, pain
8 Bajardi	Cited by Davis <sup>1</sup>	White	10	F	?	Congenital	Masseter	Excision, recovery	Diffuse cavernous angioma, no pain phleboliths
9 Bajardi	Cited by Davis <sup>1</sup>	White	Young	F	?	2 years	Sixth external intercostal	Excision, recovery	Diffuse cavernous angioma, endothelium of capillaries connected with that of cavernous spaces, pains
10 Bajardi	Cited by Davis <sup>1</sup>	White	22	F	?	12 years	Flexor longus digitorum of foot large as pigeon's egg	Excision, recovery	Capillary, arterial, cavernous angioma, pain, tibial nerve and artery in tumor, diagnosis, cold abscess
11 Baumgartner		White	69	F	None	Since youth	Muscles tongue	Cut twice, improved	Cavernous angioma, pain since youth phleboliths, in later years lip involved, tongue atrophied and blue
12 Bayha	Cited by Davis <sup>1</sup>	White	25	F	?	10 years	Triceps size of hen's egg	Excision, recovery	Capillary venous angioma
13 Bayha	Cited by Davis <sup>1</sup>	White	17	M	?	3 years	Trapezius latissimus dorsi, size of palm, 4 cm thick	Excision, recovery	Capillary venous angioma, could not breathe deeply, diagnosis, cold abscess, tuberculous
14 Bayha	Cited by Davis <sup>1</sup>	White	5	?	?	2 years	Supinator longus, 10 cm long	Excision, recovery	Cavernous angioma, phleboliths
15 Bayha	Cited by Davis <sup>1</sup>	White	18	M	?	Congenital	Vastus internus	Excision, recovery	Cavernous angioma, pain impossible to bend knee disturbance of gait
16 Belloward	Cited by Davis <sup>1</sup>	White	?	?	?	Congenital	Sacro-lumbar muscles	?	
17 Benard and Lamy		White	13	M	None	2 years	Vastus internus, size of hen's egg	Excision, recovery	Diffuse cavernous angioma, pain two years, intense, beginning with grip, atrophy of thigh, flexion checked, diagnosed deep seated angioma, skin discolored
18 Benard	Cited by Davis <sup>1</sup>	White	?	?	?	Congenital	Vastus externus	?	
19 Benard	Union med. Paris 1861	?	?	?	?	?	Vastus internus	?	

	Cited by Davis <sup>1</sup>	White	?	?	?	?	Congenital	Muscles of back size of almond	Excision recovery	(cavernous angioma blood and thrombi in the cavity & no muscle fibers in septum)	(cavernous angioma phlebotomy)
20 Berger	Cited by Davis <sup>1</sup>	White	?	?	?	?	?	Flexor carpi ulnaris trapezius	Excision recovery		
21 Berger	Cited by Davis <sup>1</sup>	White	?	?	?	?	?	Triceps	?		
22 Bilioth	Cited by Davis <sup>1</sup>	White	?	?	?	?	?	Latissimus dorsi	Excision recovery		
23 Biehat	Cited by Davis <sup>1</sup>	?	?	?	?	?	?	Detoid	Excision recovery		
24 Billroth	Cited by Davis <sup>1</sup>	?	?	?	?	?	?	Gemellus externus	Excision recovery		
25 Blane and Pclou	Cited by Lesko <sup>1</sup> These de Geneve, 1911	White	23	F	?	?	?				
26 Boeckel	Cited by Davis <sup>1</sup>	White	?	?	?	?	?	Quadriceps femoris	Excision recovery		
27 Bonnet	Cited by Davis <sup>1</sup>	White	21	M	?	?	?	Vastus lateralis size of little fin ger 4 cm long	Excision recovery		
28 Bosolino	Cited by Davis <sup>1</sup>	White	17	M	?	?	?	Rectus lateralis of right leg size of bean	Excision recovery		
29 Blanchet	Arch Ital chir 15 101 (Jan) 1920	White	20	F	?	?	?	Vastus lateralis	Excision recovery		
30 De Bugecher <sup>1a</sup>		White	?	?	?	?	?	Detoid triceps	Excision recovery		
31 Le Gros Clark 32 Coletti	Cited by Davis <sup>1</sup> Cited by Davis <sup>1</sup>	White White	?	?	?	?	?	Latissimus dorsi trapezius	Excision recovery		
33 Collin <sup>2</sup>		White	22	M	?	?	?	Biceps femoris Vastus lateralis	Excision recovery		
34 Collin <sup>2</sup>		White	13	F	?	?	?	Gastrocnemius size of walnut	Excision recovery		
35 Coote, H	Cited by Davis <sup>1</sup>	White	?	F	?	?	?	Detoid size of walnut	Excision recovery		
36 Cornelioup	Cited by Davis <sup>1</sup>	White	18	M	?	?	?	Vastus lateralis	Excision recovery		
37 Graybill <sup>1</sup>	Cited by Davis <sup>1</sup>	White	?	F	?	?	?	Biceps pectoral major coraco brachialis branch alis anticus	Excision recovery		
38 Davis <sup>1</sup>		White	12	F	?	?	?	Triceps anticus extensor indicis dilatator longus peroneus tertius	Excision recovery		
39 Davis <sup>1</sup>		White	23	M	?	?	?	Masselet brach antoi	Excision recovery		

(cavernous angioma blood and thrombi in the cavity & no muscle fibers in septum)

(cavernous angioma phlebotomy)

Diffuse cavernous angioma

(cavernous angioma skin no muscle phlebotomy)

Simple cavernous angioma atrophy of muscle & epidermis with out cavernous part

(cavernous angioma skin no muscle phlebotomy)

Simple cavernous angioma atrophy of muscle & epidermis with out cavernous part

(cavernous angioma skin no muscle phlebotomy)

Simple cavernous angioma atrophy of muscle & epidermis with out cavernous part

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(cavernous angioma skin no muscle phlebotomy)

Simple cavernous angioma atrophy of muscle & epidermis with out cavernous part

(cavernous angioma skin no muscle phlebotomy)

TABLE 1—Table of 212 Cases—Continued

Author	Reference	Color	Age	Sex	Trauma	Duration of Tumor	Location and Size	Therapy and Result	Type, Symptoms, Comment
40 Davis <sup>1</sup>		White	5	M	None	Congenital	External, internal, oblique, abdominal, 8 by 5 cm	Excision, recovery	Diffuse cavernous angioma phleboliths, pain, diagnosed skin over tumor was bluish
41 Davis <sup>1</sup>		White	17	M	10 years	1 year	Flexor digitorum sublimis and profundus, intermuscular tissue	Partial excision, recovery	Diffuse venous angioma, phleboliths pain, diagnosis between tuberculosis synovitis and angiomatous tumor, skin normal
42 Davis <sup>1</sup>		White	25	F	None	14 years	Gastrocnemius, soleus	Excision recovery	Diffuse cavernous angioma, pain for two months, adipose tissue replaces muscle, talipes equinus, diagnosed chronic myositis
43 Davis <sup>1</sup>		White	18	F	None	3½ years	Vastus internus, 10 by 4 cm	Excision recovery	Circumscribed cavernous angioma, slight pains, operated on twice recurrence three months, diagnosis, benign tumor
44 Delangere	Arch. pour de chir. Paris, 1923	White	41	F	Yes	24 years	Extensor of thumb	Excision recovery	Cavernous angioma, pain for few years ulcerated for past two years
45 Delangere	Cited by Davis <sup>1</sup>	?	?	?	?	?	Flexors of forearm	?	
46 Demarquay	Cited by Davis <sup>1</sup>	White	28	F	?	9 years	Supinator longus size of hazelnut	Excision recovery	Encapsulated cavernous angioma pain for nine years unable to extend arm diagnosed neuroma
47 Demarquay	Cited by Davis <sup>1</sup>	?	?	?	?	?	Flexor sublimis and profundus digitorum	Excision recovery	Rectile tissue
48 Demarquay	Cited by Davis <sup>1</sup>	White	29	M	?	?	Semimembranosus	Excision, recovery	Cavernous angioma
49 Denonvilliers	Cited by Davis <sup>1</sup>	White	?	?	?	?	Rectus femoris	?	Cavernous angioma skin normal no phleboliths
50 Deutschlander	Munchen. med. Wchnschr. 47 2-93 1912	White	?	F	?	?	Quadriceps	Partial excision, recovery	
51 Diefloff <sup>1*</sup>		White	22	M	None	Years	Extensor carpi radialis 8 by 4 cm	Excision, recovery	Cavernous angioma, phlebolith about size of pea, pain gradually increasing, skin normal
52 Donati	Cited by Davis <sup>1</sup>	White	25	F	?	3 to 4 years	Soleus	Excision recovery	Diffuse cavernous angioma pain for three or four years, skin normal loss of function in leg
53 Dunn	Ann Surg 82 880 (Dec.) 1925	White	17	M	None	1 year	Serratus magnus	Excision recovery	Cavernous angioma, phleboliths revealed accidentally by x-ray picture as patient came for another ailment, pain intermittent
54 Dunn	Cited by Davis <sup>1</sup>	White	15	F	?	4 years	Vastus internus, synovial membrane of knee	Excision, recovery	Cavernous angioma, pains, unable to bend knee
55 Dunn	Cited by Davis <sup>1</sup>	White	Young	F	?	?	Knee joint and muscles around it	Excision recovery	Diffuse cavernous angioma skin normal
56 Dunn	Cited by Davis <sup>1</sup>	White	24	M	?	3 months	Triceps anconeus synovial membrane	Excision recovery	Cavernous angioma containing much fat
57 Dunn	Cited by Davis <sup>1</sup>	?	?	?	?	?	Gracilis	Excision, recovery	Cavernous angioma

58 Day	Cited by Davis <sup>1</sup>	?	?	?	?	?	Since youth	Thor of forearm	Excision recovery	Muscular angioma
59 Linster	Wien klin Wochenschr 269, 1922	White	19	Y	None	None	recd rapid growth	Rhinoid minor	Excision recovery	Excision recovery
60 Fournel	Cited by Davis <sup>1</sup>	White	12	M	?	?	Conc. ult d	Sartorius	Excision recovery	Excision recovery
61 Tilt/scho	Cited by Davis <sup>1</sup>	White	9	T	1 1/2 years before	1 1/2 years	1 1/2 years	Soleus minorus	Excision recovery	Excision recovery
62 Turkotol	Cited by Davis <sup>1</sup>	White	23	M	?	?	Conc. ult d	Short muscle of foot	Excision recovery	Excision recovery
63 Lunnau <sup>8</sup>		White	16	M	None	None	10 years gradual	Gastrocnemius	Excision recovery	Excision recovery
64 Lunnau <sup>8</sup>		White	9	M	None	None	Conc. ult d	Trapezoidals major subcapitularis	Excision recovery	Excision recovery
65 Lunnau <sup>8</sup>		White	18	T	1 year before tumor appeared	1 year	1 year	Muscles of hypopharynx	Excision recovery	Excision recovery
66 Glass	Deutsche med Wochenschr 117, 1921	White	70	T	None	None	1 1/2 years	Abductor pollicis size of hazelnut	Excision recovery	Excision recovery
67 Germ	Cited by Davis <sup>1</sup>	White	20	T	?	?	18 years	Muscles of major size of nut	Excision recovery	Excision recovery
68 Germ	Cited by Davis <sup>1</sup>	White	15	M	16 years before	16 years	16 years	Interossei dorsales major	Excision recovery	Excision recovery
69 Gold <sup>10</sup>		White	10	T	7 years	7 years	15 years	Flexor carpi ulnaris size of hazelnut	Excision recovery	Excision recovery
70 Gold <sup>10</sup>		White	31	T	None	None	1 year rapid growth three months	Muscles of forearm 2 by 1 1/2	Excision recovery	Excision recovery
71 Gold <sup>10</sup>		White	10	T	1 years	1 years	3 years	Flexor carpi ulnaris	Excision recovery	Excision recovery
72 Germ <sup>11</sup>		White	23	T	10 years	10 years	10 years	Trapezius dorsalis	Excision recovery	Excision recovery
73 Gross	Cited by Davis <sup>1</sup>	White	?	T	?	?	?	Trapezius posticus inferior twelfth rib	Excision recovery	Excision recovery

TABLE 1—Table of 212 Cases—Continued

Author	Reference	Color	Age	Sex	Fracture	Duration of Tumor	Location and Size	Therapy and Result	Type	Symptoms	Comment
74 Gussenbaur	Cited by Davis <sup>1</sup>	?	?	?	?	?	Quadriceps femoris	?			
75 Gussenbaur	Cited by Davis <sup>1</sup>	?	?	?	?	?	Abdominal muscles	?			
76 Gussenbaur	Cited by Davis <sup>1</sup>	?	?	?	?	?	Extensor quadriceps	?			
77 Guyot and Jeanne		White	18	F	None	3 years	Soleus peroneus	Excision, recovery			Cavernous angioma, appeared after grip of average intensity and was diagnosed phlebitis pain which increased after immobilization, no phleboliths
78 Harddown	Cited by Davis <sup>1</sup>	White	23	M	?	3½ years	Quadriceps femoris	Excision, recovery			Diffuse cavernous angioma pain, unable to bend knee, diagnosis, tu berculosis
79 Hilde	Cited by Davis <sup>1</sup>	White	12	M	?	Congenital	Lower extremity	Electrolysis, improved			Diffuse cavernous angioma skin in volved, phleboliths
80 Heinkel	Cited by Davis <sup>1</sup>	?	?	?	?	?	Upper arm, size of goose egg	Excision, recovery			Diffuse cavernous angioma, subfascial
81 Henoque	Cited by Davis <sup>1</sup>	?	?	?	?	?	Soleus	?			
82 Horsell	Cited by Davis <sup>1</sup>	White	21	F	?	6 years	Biceps femoris semimembranosus, semitendinosus	Partial excision, recovery			Cavernous angioma pains, contractures leg could not be extended completely, diagnosis, neurofibroma
83 Hulke	Cited by Davis <sup>1</sup>	White	Small child	?	?	?	Trapezius, sternocleidomastoid	?			
84 Hustin	J de chir et ann Soc beige de chir II 307, 1911	White	24	M	3 years	3 years	Quadriceps femoris, size of orange	Excision, recovery			Cavernous angioma, skin normal, no phleboliths tumor grew with increasing pain, puncture gave blood
85 Jorgle <sup>4</sup>		White	10	M	None	Congenital	Muscles of left forearm	Seven partial excisions, improved			Cavernous angioma, bluish spot in skin, incised and bled freely, tumor lobulated, no pain, some loss of function
86 Karawski	Cited by Davis <sup>1</sup>	?	?	?	?	?	Trapezius, deep cervical muscles	?			
87 Karawski	Cited by Davis <sup>1</sup>	?	?	?	?	?	Trapezius	?			
88 Ken	Cited by Davis <sup>1</sup>	White	12	M	7 years	7 years	Extensor hallucis brevis flexor	Excision, recovery			Cavernous angioma
89 Keller	Cited by Davis <sup>1</sup>	White	24	F	?	Congenital	hallux longus	Excision, recovery			
90 Keller	Cited by Davis <sup>1</sup>	White	20	F	?	?	Biceps femoris, semimembranosus	Excision, recovery			Cavernous angioma, pains, leg could not be completely extended, lump
91 Krimmson	Cited by Davis <sup>1</sup>	White	14	F	?	?	size of orange	Excision, recovery			
92 Krimmson <sup>13</sup>	Cited by Davis <sup>1</sup>	White	14	F	?	?	Deep muscles of back	Excision, recovery			
		White	14	F	None	3 years puffiness	Triceps femoris	Excision, recovery			Cavernous angioma, phleboliths
		White	14	F	None	3 years puffiness	Vastus internus	Excision, recovery			Cavernous calcified angioma, diagnosed by X ray, pains
											Cavernous angioma pain with remissions for three years no tumor seen before operation, diagnosed tuberculosis and syphilis

		White	12	T	None	None	None seen	Vastus externus	Excision recovery	Cavernous angioma pain so severe for three or four years that she was unable to walk under other tumor palpable in normal nerve was excised in the tumor
93 Kirmleson <sup>11</sup>		White	13	T	?	?	13 years	Biceps brachii, size of apple	Excision recovery	Incapacitated cavernous angioma pain in bony spicule found limited
94 Kolaczek	Cited by Davis <sup>1</sup>	White	16	M	?	?	3 months	Biceps femoris size of pigeon's egg	Excision recovery	Diffuse simple angioma extensive fatty degeneration of muscle
95 Kolaczek	Cited by Davis <sup>1</sup>	White	17	T	?	?	7 months	Rhomboid size of hand	Excision recovery	Cavernous angioma diagnosed correctly
96 Kolaczek	Cited by Davis <sup>1</sup>	White	21	M	?	?	5 years	Muscle size of date	Excision recovery	Circumcised cavernous angioma pain diagnosed correctly
97 Kolaczek	Cited by Davis <sup>1</sup>	White	23	T	?	?	9 years	Biceps femoris	Excision recovery	Diffuse cavernous angioma phlebolytic pains distal leg 15 cm longer complete extension of leg impossible flexion of foot restricted
98 Kolaczek	Cited by Davis <sup>1</sup>	White	20	M	?	?	?	Vastus externus and extensor digitorum brevis	?	Diffuse cavernous angioma
99 Teyal and Vinnny	Cited by Levy kof, These de Geneve 1911	?	?	?	?	?	?	?	Excision recovery	Capillary and cavernous angioma
100 Teyal	Cited by Davis <sup>1</sup>	White	9	T	?	?	?	?	Excision recovery	Cavernous angioma pain on pressure on posterior tibial nerve movement restricted per equinus diagnosed as neuroma
101 Teyal	Cited by Davis <sup>1</sup>	White	?	M	?	?	?	Semimembranosus size of fist 18 cm	Excision recovery	Cavernous angioma multiple
102 Teyal	Cited by Davis <sup>1</sup>	White	10	M	None	None	Congenital	Semimembranosus	Excision recovery	Circumcised cavernous angioma
103 Teyal	Cited by Davis <sup>1</sup>	White	10	M	?	?	13 years	Semimembranosus	Excision recovery	Pulsation in early stage pain little if any diagnosed as a solid tumor
104 Tucke	Cited by Davis <sup>1</sup>	?	?	?	?	?	?	Semimembranosus	?	Cavernous angioma phleboliths
105 Tucke	Cited by Davis <sup>1</sup>	?	?	?	?	?	?	?	Excision recovery	phleboliths, itching and burning movement restricted diagnosed correctly
106 Tucke	Cited by Davis <sup>1</sup>	?	?	?	?	?	?	Superficial flexors of forearm	Excision recovery	Unresected angioma phleboliths pain formation X-ray diagnosis of bone tumor
107 Mahar	Cited by Davis <sup>1</sup>	White	12	F	?	?	10 years	Pronator, quadriceps, 6 by 3 cm	Excision recovery	Cavernous angioma
108 Malsomawe	Cited by Davis <sup>1</sup>	?	?	?	?	?	?	Deep cervical muscles	?	Cavernous angioma skin bluish no phleboliths no pain swelling began at thumb and gradually involved forearm
109 Marchetti	Reforma med 26 1011, 1910	White	13	T	None	None	5 years	Muscles of arm and hand	Amputation recovery	Cavernous angioma center ossified extension of knee and dorsal flexion of foot restricted
110 Marchetti	Cited by Davis <sup>1</sup>	White	26	M	Yes	Yes	After Injury	Gastrocnemius	Excision recovery	Cavernous angioma, completely compressible
111 Marchetti	Cited by Davis <sup>1</sup>	White	20	M	?	?	?	Rectus abdominis size of hen's egg	Excision recovery	Cavernous angioma, completely compressible
112 Mazzoni	Cited by Davis <sup>1</sup>	White	?	?	?	?	?	Triceps brachialis	?	Cavernous angioma
113 Mazzoni	Cited by Davis <sup>1</sup>	White	2	M	None	None	Congenital	Triceps brachialis	Excision recovery	Cavernous angioma

TABLE 1—Table of 212 Cases—Continued

Author	Reference Cited by Davis <sup>1</sup>	Color	Age	Sex	Trauma <sup>2</sup> ?	Duration of Tumor Some time	Location and Size	Therapy and Result	Type; Symptoms, Comment
114 Meyer	Cited by Davis <sup>1</sup>	White	19	M	?	Some time	Triiceps brachialis	Excision, recovery	Diffuse cavernous angioma, diagnosed as cold abscess
115 Meyer	Cited by Davis <sup>1</sup>	White	33	F	None	Congenital	Flexors of forearm	Excision, recovery	Diffuse spongy tumor, phleboliths, diagnosed as phlegmonous abscess
116 Mondor and Huet <sup>3</sup>		White	20	F	Yes	6 months	Left temporal muscle, size of walnut	Excision, recovery	Cavernous angioma, skin normal, painful on pressure, diagnosis, dermoid cyst
117 Mondor and Huet <sup>3</sup>		White	35	F	None	None seen	Left rectus muscle, size of walnut	Excision, recovery	Pain for several months and severe pain on pressure over inner edge of left rectus, more severe at menses, diagnosis, pelvic inflammatory disease, second incision made and tumor found, cavernous angioma
118 Mondor and Huet <sup>3</sup>		White	31	M	5 years	5 years	Left ilio-oblique, size of orange	Excision, recovery	Encapsulated angioma, afferent vessel to tumor, numerous arterioles in tumor, severe pain for last three months, puncture gave blood, tumor at edge of seventh rib, contracture of abdomen caused tumor to be come larger
119 Mondor and Huet <sup>3</sup>		White	20	M	None	6 years	Latissimus dorsi	Excision, recovery	Cavernous angioma diagnosed lipoma and at operation there was so much hemorrhage that closure was made second operation two months later
120 Monzardo	Cited by Davis <sup>1</sup>	White	18	F	None	Congenital	Quadriceps femoris	Excision, recovery	Pain on pressure and when arm was moved
121 Morgan, et al	Cited by Davis <sup>1</sup>	White	10	F	?	Congenital	Gastrocnemius size of hen's egg	Excision, ?	Diffuse cavernous angioma, slight pain, lymph lacunae present in several places
122 Morgan et al	Cited by Davis <sup>1</sup>	White	Middle aged	F	?	?	Rectus femoris	Excision, ?	Cavernous angioma, phleboliths, pain, slightly enucleatable
123 Mount	Lyons and 16 321, 1914	White	9	F	None	4 years	Gastrocnemius	Excision, recovery	Circumscribed cavernous angioma encapsulated, erectile, diagnosed correctly
124 Muscatello	Cited by Davis <sup>1</sup>	White	9	F	?	Several months	Trapezius, size of pigeon's egg	Excision ?	Cavernous angioma, part outside of muscle encapsulated, pain after fatigue at first and finally constant, indurated nodule in upper pole
125 Muscatello	Cited by Davis <sup>1</sup>	White	18	F	None	Congenital	Quadriceps size of pigeon's egg	Excision, recovery	Simple diffuse capillary angioma diagnosed lipoma
126 Muscatello	Cited by Davis <sup>1</sup>	White	28	M	?	5 years	Serratus minor, size of fist	Excision, recovery	Arterial angioma, arterial walls thickened with smaller luminae
									Cavernous angioma, phleboliths and thrombi, diagnosed as lipoma

127	Murphy	Murphy's Clinics August, 1912 p 123	White	37	M	None	None	Gastrocnemius soleus	Seen at operation improved	Cavernous angioma deformity began to appear at age of 7, at age of 10 could not touch floor with foot when standing erect slight tender ness, phleboliths
128	Nakatomi	Cited by Davis <sup>1</sup>	Yellow	27	M	?	5 years	Gastrocnemius	Excision, recovery	Diffuse cavernous angioma pain, par tially reducible skin normal
129	Nakatomi	Cited by Davis <sup>1</sup>	Yellow	9	F	?	3 years	Gastrocnemius	Excision recovery	Diffuse cavernous angioma pain nerve trunk infiltrated pes equinus diagnosed tumour, then neuroma then angioma
130	Nakatomi	Cited by Davis <sup>1</sup>	Yellow	40	M	?	1 year	Gluteal muscles	Excision, recovery	Diffuse cavernous angioma pain pul sation in later stage
131	Nakatomi	Cited by Davis <sup>1</sup>	Yellow	23	M	?	3 years	Sacro-lumbar mus cles size of child's hand	Excision recovery	Diffuse cavernous angioma pain
132	Nakatomi	Cited by Davis <sup>1</sup>	Yellow	?	?	?	?		Excision, recovery	Diffuse cavernous angioma phleb olitis
133	Nakatomi	Cited by Davis <sup>1</sup>	Yellow	9	M	None	Congenital	Masseter	Excision, recovery	Cavernous angioma pain noted at birth then lost sight of and rap ported at age of 3
134	Nast Kolb	Cited by Davis <sup>1</sup>	White	12	F	?	7½ years	All muscles of foot and leg,	Amputation recurrence	Diffuse cavernous angioma pain nerve involved pes equinus dia gnosed angioma
135	Nelson and Hill juv.	Cited by Davis <sup>1</sup>	White	Young	F	?	?	Pronator teres radial	Excision, recovery	
136	Oller	Cited by Davis <sup>1</sup>	?	?	?	?	?	Pectoralis major Masseter	?	
137	Pantaleoni	Cited by Davis <sup>1</sup>	White	25	M	?	11 years		Excision, recovery	Cavernous angioma, no pain diag nosed as tuberculous glands
138	Pantaleoni	Cited by Davis <sup>1</sup>	White	8	F	?	3 years	Masseter	Excision, recovery	Primary muscle angioma, diagnosed as cold abscess
139	Pearl	Cited by Davis <sup>1</sup>	White	21	?	?	2 years	Masseter	Excision recovery	Cream-colored cavernous angioma some thrombi as large as cherry pit, no pain
140	Petersen	Cited by Davis <sup>1</sup>	White	11	F	?	3 years	Tensor quadrat iceps large as fist	Excision, recovery	Cavernous angioma, phleboliths diagnosed lipoma
141	Petersen	Cited by Davis <sup>1</sup>	White	7	M	?	5 years	Calf muscles	Excision recovery	Diffuse cavernous angioma pain pes equinus complete extension of knee impossible
142	Pillet	Cited by Davis <sup>1</sup>	White	11	M	?	?	Teg and psoas muscles	Partial excision recovery	Diffuse cavernous angioma pain numerous nevi, nerve infiltrated
143	Pupovac	Cited by Davis <sup>1</sup>	White	15	M	?	5 years	Muscles of thigh	Excision, recovery	Cavernous angioma
144	Pupovac	Cited by Davis <sup>1</sup>	White	11	F	?	6 years	Quadriceps fi nors, size of egg	Excision recovery	Cavernous angioma no pain diag nosed lipoma fibrous tangle
145	Pupovac	Cited by Davis <sup>1</sup>	White	17	F	None	Congenital	Abdominal mus cles, 21 cm long,	Excision, recovery	Cavernous angioma, no phleboliths
146	Putti	Cited by Davis <sup>1</sup>	White	33	M	?	Since child hood	Gastrocnemius	Excision, recovery	Cavernous angioma pain small cal cious contractions, pes equinus diagnosed neurofibroma
147	Putti	Cited by Davis <sup>1</sup>	White	29	F	19 years	19 years	Gluteus medius maximus, lumbroc nemus muscles of foot	Excision, recovery	Cavernous angioma pain pes equinus valvose veins diagnosed correctly



TABLE 1—Table of 212 Cases—Continued

Author	Reference	Color	Age	Sex	Trauma	Duration of Tumor	Location and Size	Therapy and Result	Type, Symptoms, Comment
118 Ponce	Cited by La- Garde 1911	White	10	M	Yes		Quadriceps femoris	?	Cavernous angioma, two other tu- mors found in triceps and supinator longus
119 Quenn	Cited by Davis <sup>1</sup>	?	?	?	?	?	Pectoralis major	Excision, ?	Multiple angioma
120 Ribold	Cited by Davis <sup>1</sup>	?	?	?	?	?	Thenar eminence	Excision, ?	Diffuse cavernous angioma, pain,
121 Ricketts	Cited by Davis <sup>1</sup>	White	17	F	None	8 months	Latissimus dorsi, 10 by 8 cm	Excision, recovery	diagnosed sarcoma
122 Richards and Holt	Cited by Davis <sup>1</sup>	White	28	F	?	3 years	Epiptrochlear mus- cles, size of chestnut	Excision, recovery	Cavernous angioma, phleboliths, pain, diagnosed sarcoma
123 Ricketts	Cited by Davis <sup>1</sup>	?	?	?	?	?	Triceps brachialis	Excision, recovery	Cavernous angioma
124 Rietkus	Cited by Davis <sup>1</sup>	White	14	F	4 years	4 years	Tibialis posterior, flexor digitorum longus, flexor hallucis longus, plantaris	Partial excision, recurrence	Diffuse cavernous angioma, pain tibial nerve infiltrated, complete ex- tension of knee impossible pes equinus, amputation eight months later
125 Rietkus	Cited by Davis <sup>1</sup>	White	32	M	None	8 years	Sacrospinal mus- cles, size of hand	Excision, recovery	Cavernous angioma, pain, no phle- boliths
126 Rigaud	Cited by Davis <sup>1</sup>	White	45	F	?	1 year	Muscles of tongue, large as grape	Excision, recovery	Cavernous angioma, compressible mucous membrane intact
127 Rie, and	Cited by Davis <sup>1</sup>	?	?	?	?	?	Muscles of back	Excision, recovery	Cavernous angioma
128 Rigaud	Cited by Davis <sup>1</sup>	?	?	?	?	?	Muscles of forearm, size of almond	Excision, recovery	Cavernous angioma, phleboliths
129 Rietchl	Cited by Davis <sup>1</sup>	?	?	?	?	?	Muscles of forearm, size of almond	?	Hematolymphangioma mixtum
130 Rietchl	Cited by Davis <sup>1</sup>	?	?	?	?	?	Flexors of forearm Vastus internus	?	Hematolymphangioma mixtum here the pure primary lymphangiomatous character could be established with certainty
131 Roberts	Cited by Davis <sup>1</sup>	White	17	F	?	?	Quadriceps femoris size of fist	Excision, recovery	Cavernous angioma
132 Robin	Cited by Davis <sup>1</sup>	?	?	?	?	?	Vastus internus, size of cherry	Excision, recovery	Cavernous angioma, large veins, 0.1 to 0.3 cm in size, connected with cavities
133 Rocher and Taton	Cited by Davis <sup>1</sup>	White	52	M	Yes	32 years	Ocularis oculi	Excision, recovery	Circumscribed cavernous angioma, pain, diagnosed as dermoid cyst
134 Romati	Bull d sc med 96 120, 1924	White	23	M	4 years	4 years	Triceps femoris	Excision, recovery	Cavernous angioma, pain for four years, phleboliths skin normal
135 Romati	Bull d sc med 96 120, 1924	White	24	M	None	18 years	Latissimus dorsi	Excision, recovery	Cavernous angioma, pain for five years, no phleboliths, skin normal, some limitation of motion
136 Roschano	Cited by Davis <sup>1</sup>	White	22	M	None	Congenital	Rectus abdominis	Excision recovery	Cavernous angioma, diagnosed as lipoma
137 Scudro	Wien med Wehn-schr 1903	White	30	M	7 years	7 years	Temporal, size of nut	?	Cavernous angioma, phleboliths, pain, pulsation at first

168 Scum	Cited by Davis <sup>1</sup>	White	16	M	5 years	5 years	Quadriceps femoris	1	Recovery	Cavernous aneurysm, disappeared with elevation of limb
169 Scarfata		White	8	M	None	Early infancy	Biceps brachii size of mandarin	1	Recovery	Cavernous aneurysm, no pain in creased vascularity in the skin over the tumor size of pea when first noted eight years before no pain phlebolytic puncture gave blood diagnosed correctly
170 Scurr	Arch Clin chir 10: 1015 1871	White	21	F	20 years	10 years	Vastus externus	1	Recovery	Cavernous aneurysm varicosities in skin over tumor began to grow rapidly seven years ago when pain set in
171 Shaw	Cited by Davis <sup>1</sup>	White	17	F	None	Concurrent	Isthmus dorsalis sciatissimus	1	Recovery	Circumscribed cavernous aneurysm no pain
172 Solcail	Tschi f. orthop Chir 10: 110, 1912	White	16	M	7 years	7 years	Rectus femoris	1	Recovery	Capillary cavernous aneurysm pain sense of tension walling, difficult contraction of knee joint no phlebolytic diagnosed neurofibroma
173 Steele	Cited by Davis <sup>1</sup>	White	1	M	None	Concurrent	Quadriceps femoris	1	Recovery	Cavernous aneurysm
174 Stomham	Cited by Davis <sup>1</sup>	?	?	?	?	?	Brachia	1	Recovery	Cavernous aneurysm
175 Strach	Cited by Davis <sup>1</sup>	White	19	M	?	15 years	Masseter	1	Recovery	Cavernous aneurysm, slight pain as man's thumb
176 Summers	Cited by Davis <sup>1</sup>	White	13	M	8 years	8 years	Gluteus maximus	1	Recovery	Cavernous aneurysm no pain
177 Sutter	Cited by Davis <sup>1</sup>	White	24	M	None	Concurrent	Thin muscles	1	Recovery	Aneurysm after second operation
178 Sutter	Cited by Davis <sup>1</sup>	White	20	F	?	11 years	Soleus size of bean	1	Recovery	Diffuse cavernous aneurysm, muscle in infiltrated with fat pain
179 Sutter	Cited by Davis <sup>1</sup>	White	12	M	?	3 years	Soleus	1	Recovery	Diffuse cavernous aneurysm, somewhat painful
180 Sutter	Cited by Davis <sup>1</sup>	White	28	M	None	Concurrent	Vastus internus size of pigeon's egg	1	Recovery	Cavernous aneurysm pain extension of elbow restricted, diagnosed
181 Tacknat	Cited by Davis <sup>1</sup>	White	20	M	?	5 months	Supinator longus size of goose's egg	1	Recovery	Primary diffuse aneurysm of muscle
182 Tacknat	Cited by Davis <sup>1</sup>	White	21	F	?	6 years	Quadriceps size of hen's egg	1	Recovery	Cavernous aneurysm partially circumscripted
183 Tacknat	Cited by Davis <sup>1</sup>	White	21	M	?	10 years	Biceps brachii	1	Recovery	Cavernous aneurysm
184 Tacknat	Cited by Davis <sup>1</sup>	White	17	F	?	?	Semimembranosus	1	Recovery	Intelle
185 Thome	Cited by Davis <sup>1</sup>	White	22	M	?	Several months	Isthmus dorsalis	1	Recovery	Cavernous aneurysm no pain
186 Thlman	Cited by Davis <sup>1</sup>	White	12	F	?	?	Sciatissimus dorsalis	1	Recovery	Circumscribed cavernous aneurysm bounding squaring, phlebolytic inactive infiltrated
187 Thlman	Cited by Davis <sup>1</sup>	?	?	?	?	?	Supraclavicular	?	Recovery	Arteriovenous aneurysm, (rhabdomyoma)
188 Thlman	Cited by Davis <sup>1</sup>	?	?	?	?	?	Stomach	1	Recovery	Cavernous aneurysm, two weeks before admission a red spot appeared on the calf with pain affected by touch no impairment of motion
189 Van der Spil	Cited by Davis <sup>1</sup>	?	?	?	?	?	Quadriceps femoris	1	Recovery	
190 Vautin	Cited by Davis <sup>1</sup>	?	?	?	?	?	Muscles of calf	1	Recovery	
191 Vithusen	Norsk Med. Tidsskrift 11: 789 1899	White	19	M	None	5 or 6 years	Muscles of calf larger than fist	1	Recovery	

TABLE 1—Table of 212 Cases—Continued

Author	Reference	Color	Age	Sex	Trauma	Duration of Tumor	Location and Size	Therapy and Result	Type, Symptoms, Comment
192 Vernon <sup>1</sup>	Chir d org di movimento S. 529 (Aug) 1924	White	20	M	None	Congenital	Muscles of leg	Amputation, re- covery	Diffuse cavernous angioma, intense pain on standing and sudden relief on lying down, diagnosed osteo- myelitis
193 Vannay	Cited by Davis <sup>1</sup>	White	26	F	?	8 years, re- currence in 4 years	Vastus internus, small	Excision, recur- rence	Cavernous angioma, pain, phlebo- liths, unable to extend leg, recovery after second operation
194 Vincent	Cited by Davis <sup>1</sup>	White	12	M	?	2 years	Pectoralis major, size of nut	Excision, recovery	Circumscribed cavernous angioma, easily enucleable, structure similar to erectile tissue
195 Virehow	Cited by Davis <sup>1</sup>	?	?	?	?	?	Thenar eminence	Excision, recovery	Cavernous angioma
196 Volkman	Cited by Davis <sup>1</sup>	?	?	?	?	?	Flexor digitorum profundus	?	
197 Wakeley <sup>14</sup>		White	24	F	None	6 years	Tibialis anticus	Excision, recovery	
198 Wakeley <sup>14</sup>		White	12½	M	None	7 years	Vastus externus	Excision recovery	Cavernous angioma, pain and itching, most severe at night, x-ray showed phleboliths, much hemorrhage at operation, wound picked
199 Wimeck	Cited by Davis <sup>1</sup>	White	28	F	?	12 years	Rectus abdominis, large as palm	Excision, recovery	Cavernous angioma, painful, phlebo- liths seen in x-ray, movable in tu- mor, pain in knee off and on for seven years, tumor tended to dis- appear on flexion, diagnosed
200 Wharton <sup>15</sup>		White	1	M	None	Congenital	Pectoral muscle and shoulder	Cauterization, recovery	Angioma simplex, hypertrophieum diagnosed fibrosarcoma and der- moid cyst
201 Wump <sup>16</sup>		White	70	F	None	Many years	Gluteal muscles	Partial excision, recovery	Cavernous angioma, well after several treatments
202 Case 1		White	69	M	None	3 months	Masseter size of pea	Excision, recovery	Cavernous angioma, skin became in- volved in later years, no record of pain, phleboliths
20, Case 2		White	23	M	20 years	20 years	Gastrocnemius, adductor longus	Amputation, re- covery	Cavernous angioma, pain, contrac- ture and deformity, two operations attempted to correct deformity gangrene after second operation, amputation, 1 second amputation was done to relieve contracture and give a weight bearing stump one calcified area found when specimen was examined after operation, origi- nal diagnosis was nondeforming clubfoot correct diagnosis at last operation

201 Case 3	White	25	M	None	7 years	Pilonous bony flexor longus bulbous	1 x 1.5 cm recovery	(asymptomatic) began with pain 4-5 years ago pain most severe on standing or walking swelling disappeared when patient lay down no phlebectasis no impairment of function diagnosed correctly (asymptomatic) seven years ago it was the size of an egg twelve years ago it was partially excised pain which began after on set persisted some limitation of motion because of pain skin shiny over tumor no phlebectasis diag- nosed function
205 Case 4	Black	31	F	None	Congenital	1 x 1.5 cm polypoid	1 x 1.5 cm recovery	(asymptomatic) painless although patient thought arm was large due long, damp weather diagnosed cor- rectly
206 Case 5	White	12	F	None	3 years	Biceps brachii size of egg	1 x 1.5 cm recovery	(asymptomatic) painless although patient thought arm was large due long, damp weather diagnosed cor- rectly
207 Case 6	White	21	F	None	10 years	Biceps femoris	1 x 1.5 cm recovery	(asymptomatic) after an approx- imately a swelling appeared slightly annoying but never painful during past two years tumor had become tender no phlebectasis diag- nosed lipoma well after one year
208 Case 7	White	11	F	2 years	9 years	Gastrocnemius	Partial excision improved	(asymptomatic) pain and limp began two years after injury con- tinued of hamstring muscles and tendo achillis phlebectasis two oper- ations and radium used with only slight improvement last report pa- tient still disabled and suffering old and diagnosed thaladomyoma
209 Case 8	White	29	M	6 years	6 years	Masseter size of walnut	1 x 1.5 cm recovery	(asymptomatic) six years ago wounded by sharp object in a base hospital and discharged with a swelling pain began one month ago x-ray showed iron and phlebectasis diagnosed as a lipoma or cyst with sharp cut well on last report
210 Case 9	White	13	M	9 years	9 years	Semispinalis and spilius capitis size of hen's egg	1 x 1.5 cm recovery	(asymptomatic) pain for one year six months ago operated on for lipoma returned during exam- ination tumor changed in size no phlebectasis diagnosed cyst
211 Case 10	White	11	F	6 years	6 years	Soleus size of plum	1 x 1.5 cm recovery	(asymptomatic) six years ago felt pain while dancing since then there has been tenderness left calf has been a little smaller gradual limp diagnosed as hip disease and myo- sitis no phlebectasis no impairment of function
212 Case 11	White	20	F	None	9 years	Semispinalis 1 1/2 by 1 inches	1 x 1.5 cm recovery	(asymptomatic) noticed at school only pain diagnosed as lipoma and incised then thought closed again diagnosed as lipoma, phlebectasis found in specimen, no impairment of function

The cavernous spaces are of different sizes and forms. They are formed by the dilatation and fusion of the capillaries. They may be lined with endothelium and contain blood, or the lining may appear to be absent and the blood be in direct contact with the connective tissue and smooth muscle surrounding them. Around the spaces is a framework of connective tissue and smooth muscle carrying arteries and veins.

The connective tissue forms the framework of the tumor, causing variations in the spaces. The partitions of connective tissue are thick if there is an abundance of connective tissue present and thin if it is scant. The partitions are usually covered with endothelium and some are so thin that the endothelium is practically back to back. In places the partitions do not reach across the spaces forming what Verneuil called angiomatous valves. These formations seem to depend on the proliferation of the connective tissue and not on atrophy of preexisting tissue due to pressure of the blood.

Muscatello thought that the connective tissue originated from the perimysium, while Reclus and Magitot believed that it came from the adventitia of the arterioles and veins. Karyokinesis is occasionally seen in the nuclei of the connective tissue cells. Elastic tissue is seen throughout the tumor when proper staining is done.

Sometimes one sees cellulo-fatty tissue enclosing remnants of damaged muscle fibers. Sometimes the connective tissue is loose with a quantity of capillaries intermingled with muscle fibers of normal appearance.

The connective tissue is generally found with few cellular elements, but sometimes the cells are seen grouped with a great number of leukocytes, giving the impression of lymphoid formations.

In these tumors alterations appear in the arterial walls making them thicker especially than those of smaller caliber. This thickening is due to the proliferation of endothelial cells often arranged in rows. There may also be a proliferation so active as to produce a complete obstruction of the lumen of the vessel. The other layers are also hypertrophied. Sometimes there is a thickening of the middle tunic, and at other times the adventitia is greatly enlarged.

The capillaries are most important. Each capillary has a wall of its own, which may be formed of endothelium alone or may be almost arterialized. Instead of a single layer of endothelium there may be two or three layers. The lumen varies in size. According to Muscatello, the capillaries proliferate, and buds are sometimes seen coming from the walls. Sutter said that these capillaries dilate, fuse and form the cavernous spaces. Rigaud said, however, that the number of capillaries always remains the same and that the lacunae are formed by dilatation and never by fusion.

The majority of authors are of the opinion that the veins are often absent and when they do exist are scarce and have no special charac-

teristics Benard and Lamy stated that veins do participate and present arterialization of their walls. New vessels are formed with the structure of veins. The walls may be thickened or dilated and atrophied. The dilated vessel may form the irregular venous space cavities which are probably the result of obstruction. In spite of careful investigation (Bajardi, Riethus and others), satellite veins of large arteries have not been found.

Nerve fibrils and sometimes a large nerve are found in the tumor, however these are simple enclosures of normal nerves which resist destruction much better than do the muscle fibers.

Muscatello and Sutter described smooth muscle fibers, probably of vascular origin, as though the venous walls, on the disappearance of the vessel, left part of the middle tunic between the connective tissue surfaces. It predominates in some places, and many authors believe that it originates from the muscular coats of both arterioles and veins.

The muscle itself presents changes of different natures. In some areas it retains its normal aspect with clear striations and well stained nuclei. In other areas it appears as bands of uniform color, staining without its structural design. At times fatty degeneration is seen. Riethus and Ritschl believed that the fatty tissue invaded the muscle causing degeneration. Sutter believed that the fat was the result of muscle degeneration. This interpretation is the correct one as it is a well established fact that fat replaces any degenerated highly specialized tissue.

Angiomas have also been described which are surrounded by an envelop or capsule of connective tissue which Charpenay called circumscribed angiomas.

#### TREATMENT

Various treatments have been tried for the cure of angiomas of the muscle. Local applications, the insertion of setons, magnesium darts and ivory pegs, have been tried with little success. The injection of various types of cauterizing fluids, to bring about atrophy of the blood spaces through the formation of scar tissue by aseptic inflammation, has failed. Other liquids have been injected to cause coagulation of the blood in the tumor, but these have also been of little value. The substances used included boiling water, nitric acid, alcohol, tannic acid, tincture of iodine, lead acetate, ammonia, perchloride of iron and the chloride of lime. In some cases the result has been fatal, in others abscesses have formed and sloughing has occurred. Cauterization by means of the Paquelin cautery has been used to induce more rapid coagulation. Wharton<sup>18</sup> (200) cured an angioma with the galvanic cautery after several months of treatment. Heide reported a case in which the

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<sup>18</sup> Wharton H. R. Extensive Angioma of the Upper Extremity, Tr. Philadelphia Acad. Surg. 1911 vol. 13.

patient was treated by electrolysis with satisfactory results. He used a current of from 30 to 40 milliamperes for three or four minutes at each treatment over a long period of time. Treatments with the roentgen rays and radium have been tried with some success. The diagnosis in these cases, however, is always questionable unless it is verified by an exploratory operation. The method offering the best result is excision or at least partial excision. In the case of circumscribed or well limited angiomas, excision of the tumor itself will suffice. In diffuse angiomas it is necessary to remove the tumor with a good margin of healthy muscle around it in order to insure a permanent cure. This procedure is relatively easy when the tumor is small, but it presents great difficulties in the larger tumors which involve a considerable portion of an important muscle or group of muscles. In these instances various treatments may be employed in the effort to save the affected limb from amputation. Compression of the angioma, ligation of the arteries which nourish the tumor and treatments with radium or the roentgen rays can be tried. Partial or complete long continued compression of the angioma has not been satisfactory, and ligation of the nourishing vessels is, one can easily see, difficult if not entirely impossible without injuring the affected extremity as there is rarely a single afferent vessel. Radium seeds buried in the tumor and deep roentgen treatment promise the best results and may reduce the angioma so that it can be removed later. If these methods fail, amputation can be done. It is also advisable to amputate in those instances in which the tumor has damaged the extremity so much that it would be useless even if the whole tumor were removed.

#### PROGNOSIS

The prognosis as to life is excellent. The majority of angiomas of the muscle are benign. The tendency to invasion is the serious feature of these tumors and early operative intervention will aid in reducing the number of functional impairments. The question of malignancy has never been established, and the majority of angiomas of the muscle should be considered benign.

#### REPORT OF CASES

CASE 1—*Diagnosis* Intramuscular hemangioma of the masseter muscle, excision, recovery

*Clinical History*—A white man aged 69, a German, was admitted to the Johns Hopkins Hospital on Jan. 20, 1910. The past and family history were unimportant. Three months before admission the patient felt a painful lump inside of the left cheek. When first noted the growth was the size of a pea, but it gradually increased. He began to catch the mucous membrane between his teeth and finally an ulcer formed. There was no pain at the time of admission.

*Physical Examination*—The results of the examination were negative except for a ragged ulcer on the inside of the left cheek about the size of a quarter. The

floor was fissured and there was a slight inflammatory reaction around it and slight induration. It bled easily. A small mass was felt through the cheek. A diagnosis of a malignant condition was made. The Wassermann reaction and urinalysis were negative.

*Operation*—Dr. Halsted performed an operation on Jan. 22, 1910, using gas and ether anesthesia. The cheek was divided and the growth exposed. It was excised and the area was cauterized. Bleeding points were ligated and the wound on the cheek was sutured. The patient made an uneventful recovery.

*Microscopic Pathologic Changes*—The tissue was composed of numerous blood vessels and blood spaces in muscle and fat. The blood spaces were irregular in size and were lined with endothelium. In some areas there was no connective tissue between the endothelial cells of the adjoining spaces. The walls of the arteries showed an increase in the connective tissue and in the endothelium. A number of vessels had endothelium two layers thick. Some of the veins were irregular in shape with thin walls. One vein had a thick wall and was partially thrombosed. All the vessels and blood spaces were packed with blood cells. The muscle fibers in some areas had lost their nuclei and appeared as hyaline. In these areas the fibrous tissue was increased. The nuclei of the fibrous tissue in these areas were more numerous than normal. In some areas there was an infiltration of round cells.

*Subsequent History*—The patient was discharged well. No further record was obtained.

*CASE 2—Diagnosis* *Intramuscular hemangioma of the muscles of the calf and adductors of the thigh, reamputation, recovery.*

*Clinical History*—A white man, aged 23, a bookkeeper of Scotch-Irish descent, was admitted to the Johns Hopkins Hospital on Aug. 21, 1911. The past and family histories were negative. At the age of 3 the patient had a fall followed by tenderness and swelling of the right calf. After this subsided, a lump was found in the calf which did not disappear. He began to have difficulty in walking and during the next five years the deformity became so great that he walked on his toes with the heel drawn up. In addition there was flexion at the knee. Seven years after the onset, at the age of 10, he had scarlet fever and after convalescence was not able to put the heel on the floor. The condition became gradually worse until in March, 1906, fifteen years after the onset, he came to the hospital for treatment for the deformity.

There was a marked contracture of the Achilles tendon with atrophy of the calf and thigh. The knee was flexed at an angle of 45 degrees. A diagnosis of nondeforming clubfoot due to cerebral disturbance was made. An attempt to lengthen the hamstring muscles was made, but on account of excessive hemorrhage the operation was abandoned.

The patient had smallpox while in the hospital after recovering from the disease he was discharged. He returned after a month and a second operation was attempted this time around the knee. The popliteal nerve and probably the vessels were injured as gangrene set in and an amputation had to be done in the lower third of the leg. The deformity at the knee continued to increase during the following five years and the patient again came to the hospital for further treatment. He desired to get a weight-bearing stump. This was twenty years after the onset of the disease.

*Physical Examination*—The stump below the knee was atrophied and was held flexed at the knee. There was some motion in the knee joint. When the leg hung the internal saphenous vein with numerous serpentine branches became hugely



dilated, and there was enlargement of the upper half of the thigh suggesting deep-seated hemangioma

*Operation*—On Aug 25, 1911, Dr Bloodgood performed an operation, using gas anesthesia. Reamputation was done. An Esmark bandage was applied, and the stump was amputated at the junction of the middle and lower thirds of the thigh. In making the circular amputation it was found that the femoral artery and vein were smaller than normal, but the veins of the saphenous network were hugely dilated. The adductor longus was an indurated mass, and on section the muscle tissue was found to be replaced by fibrous tissue in the meshwork of which were numerous blood spots. A vertical incision was made and the adductor longus was dissected out to its origin. The mass of veins and fat around the saphenous were also removed. All bleeding vessels were ligated, the Esmarck bandage was removed and the wound was closed.

*Gross Pathology* (Dr Bloodgood)—The knee joint was normal, and there was no evidence of inflammation. There was distinct evidence of an angiomatous condition of the gastrocnemius muscle, but scar tissue had taken its place and the other muscles were replaced by fat. In the thigh the adductor longus muscle was involved down to its attachment, but no other muscles of the thigh were involved. The adductor longus was fibro-angiomatous and contained one calcified area.

*Microscopic Pathology*—The tissue was composed of loose fibrous strands in which were many large spaces lined with endothelium, some of which contained blood. These spaces were irregular in size and shape. In one space there was a mass of connective tissue covered with endothelium which was evidently a cross-section of a papillary projection. Many of these large blood spaces lacked endothelial lining. In some areas the wall of the blood space rested against muscle fibers which were hyaline and vacuolated, showing degeneration. The walls of many blood spaces contained smooth muscle. Many had thickened layers of endothelial cells so that the lumina were small. There were patches of smooth muscle scattered in the wavy fibrous tissue between the blood spaces. Some vessels showed a thickening in the fibrous layer of their walls.

In another section there were numerous voluntary muscle fibers showing degenerative changes. In other areas there was fat with areas of muscle fibers, giving the impression that the latter had been replaced by the former. In some areas there was a small round cell infiltration in the connective tissue.

*Subsequent History*—There was pain in the stump which began after twelve years, the history was otherwise negative.

*CASE 3—Diagnosis* *Intramuscular hemangioma of the peroneus brevis and flexor longus hallucis, excision, recovery*

*Clinical History*—A white man, aged 28, a merchant, a Jew, was admitted to the St Agnes Hospital on Aug 27, 1912. The past and family histories were negative. Eight years before admission the patient noted that the leg was painful. Later he found a small lump on the posterior surface of the right calf. The pain was most severe on standing or walking. There was no history of injury.

*Physical Examination*—The results were negative except for the condition of the right leg. When the patient stood, a lump about the size of a walnut appeared on the posterior surface of the calf. There was no pulsation, and the mass gave the sense of fluctuation. When the patient lay down, the mass disappeared. There was no change in the skin and no subcutaneous varicose veins were visible. The lump was compressible. Pain was chiefly in the region of the swelling and above it in the calf of the leg. No measurements were made, but the leg affected

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appeared fuller than the normal one. There were a few dilated veins in the popliteal space. A diagnosis of angioma was made.

*Operation*—On Aug. 29, 1912, Dr. Bloodgood performed an operation, using gas and ether anesthesia. The bulging area was 3 cc. above the external malleolus between the achilles tendon, the peroneal muscles and the flexor longus hallucis. A mass of dilated veins in the subcutaneous fat anastomosing with the fine veins on the achilles tendon was found. These communicated with the angioma in the peroneus brevis and the flexor longus hallucis. All this tissue was completely excised. Closure was made, and an iodiform drain was put in. An Esmarch bandage was used around the thigh. The drain was removed on the fifth post-operative day. The healing was uneventful.

*Gross Pathology* (Dr. Bloodgood)—The tissue consisted of subcutaneous varicose veins and fat, the angioma in the muscle and some normal muscle.

*Microscopic Pathology*—The sections showed the usual picture of angioma. There were blood filled spaces of irregular size and shape between the muscle bundles. The walls of these spaces were connective tissue with a lining of endothelium. In some areas there were infiltrations of small round cells suggesting inflammation. The striated muscle fibers were replaced by fat (fig. 1).

*Subsequent History*—In 1920, eight years after the operation, the patient wrote that he had pain in the region of the scar which was attributed to the scar itself. Examination failed to reveal any recurrence of the growth.

*CASE 4—Diagnosis* *Intramuscular hemangioma of the extensor pollicis, excision, recovery*

*Clinical History*—A colored woman, aged 34, a domestic, was admitted to the Johns Hopkins Hospital on May 12, 1913. The past and family histories were negative. Since childhood there had been a small lump on the anterior surface of the wrist. This had gradually grown until, seventeen years before the patient's admission, it was the size of an egg, and had become extremely painful, causing tingling in the fingers and loss of function. Twelve years before the patient's admission the lump was removed by a physician. The patient said that it looked like beef. After this operation the pain did not subside, and gradually a new lump began to appear. Because of pain the patient had little use of her fingers.

*Physical Examination*—A soft murmur was transmitted from the heart to the axilla. The results of the examination were otherwise negative except for the condition of the left upper extremity. The left arm was somewhat atrophied. There was a dark scar about 1 inch (2.5 cm.) long over the back of the wrist at the lower end of the radius. There was a swelling extending from this scar for about 10 cm. up the dorsum of the radius. The skin over the swelling was movable and a little shiny. There was no local heat. The swelling was tender, not fluctuant and was movable over the bone. There was little motion in the wrist because of tenderness, and the thumb and forefinger were practically useless. She could not make a fist. The hand was atrophied and was held in slight dorsal flexion at the wrist.

Measurements	Right	Left
Hand	22 cm	19 cm
Wrist through swelling	16.5 cm	17.5 cm
Wrist above swelling	19.5 cm	15.5 cm
Forearm	26 cm	23 cm
Arm	23.5 cm	21.5 cm

The results of urinalysis and a Wassermann test were negative. A diagnosis was made of ganglion along the tendon sheath.

*Operation*—On May 22 1913 Dr. McClure performed an excision, using ether anesthesia. An incision was made over the old scar and the present tumor. A dense mass of fibrous tissue was found which was gradually excised exposing the tumor which lay under the scar and extended for about 5 cm. up under healthy tissue. When the mass was dissected out, it was found to involve the extensor pollicis. The tumor was also found to be adherent to the capsule of the joint, and a piece of the capsule had to be removed with it. The tendon of the extensor



Fig 1 (case 3)—1, cellular connective tissue which forms the framework of the angioma, 2, irregular blood filled spaces, 3 endothelium covered walls separating the cavernous spaces, 4, solid mass of endothelial cells, 5, cross-section of one of the budding channels, 6, degenerated muscle fibers, 7, fat replacing muscle

pollicis was then sutured to the extensor indicis. Closure throughout was made with silk.

*Gross Pathology*—The specimen had a nodular appearance. The nodules were extremely dark and the tissue between was white and fibrous. On section it looked like a sponge.

*Microscopic Pathology*—There was a large amount of fibrous tissue in which were blood spaces which were irregular in size and shape. Some of these lacunae were separated by thin walls of connective tissue joined with endothelium so that it appeared as if the endothelium was back to back. Here and there were small bundles of smooth muscle. Some of the larger vessels had an increase in the fibrous tissue of their walls. In one section there was a vein with a thick wall. The muscle tissue showed degenerative changes. Figures 2 and 3 show the lacunae and connective tissue stroma. The high power gave an idea of the walls of the blood spaces. In this case the sections made did not show any areas of cellular

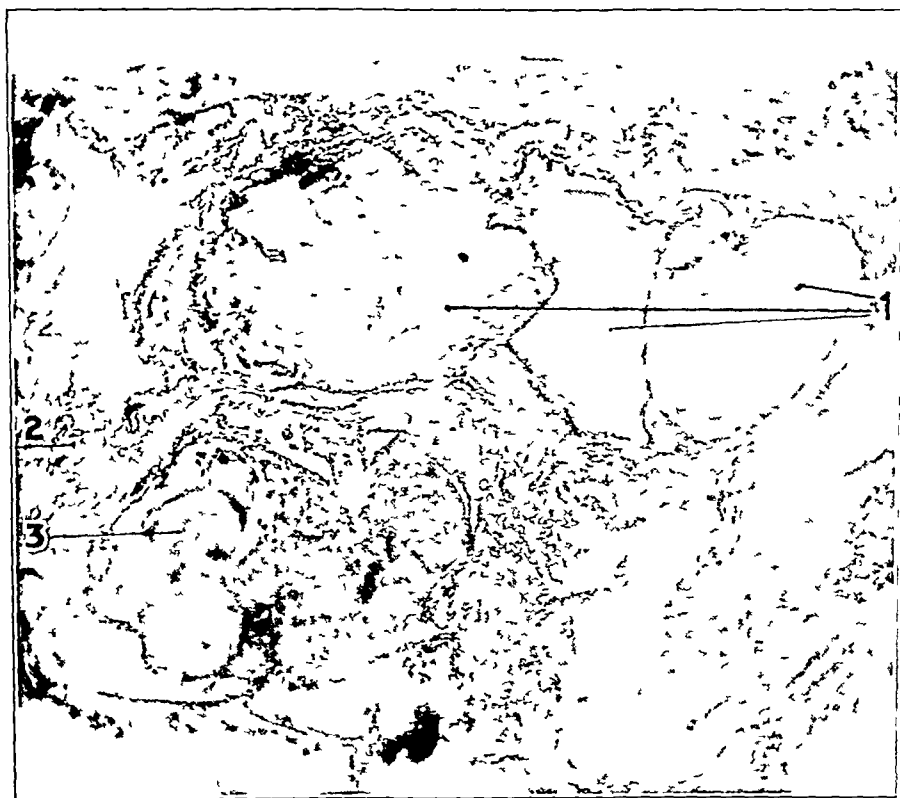


Fig 2 (case 4)—1 large lacunae filled with normal blood, 2 cellular connective tissue 3 blood channels in the connective tissue without endothelial lining

infiltration. The blood in the lacunae appeared normal. Other sections showed the blood enclosed in fibrous tissue spaces without any endothelial lining.

*Subsequent History*—The patient was discharged well. No further report could be secured.

*CASE 5—Diagnosis* Intramuscular hemangioma of the biceps brachialis  
excision recovery

*Clinical History*—A white girl, aged 12, a student, a Jew, was admitted to the Johns Hopkins Hospital on Sept 17 1915. The family and past histories were negative. Three years before admission the patient's mother noted a slight enlargement over the inner side of the upper third of the right arm. This had gradu-

ally increased without any pain or discomfort. The patient thought that the arm was lame during damp weather.

*Physical Examination*—The results were negative, except for a swelling over the biceps of the right arm. When the patient flexed her arm, the tumor became more prominent and looked like hypertrophied muscle. The skin was normal over the tumor and was not adherent. The swelling was soft, compressible, not lobulated or tender. The edges were poorly defined. There was no limitation of motion. The diagnosis was angioma of the muscle.

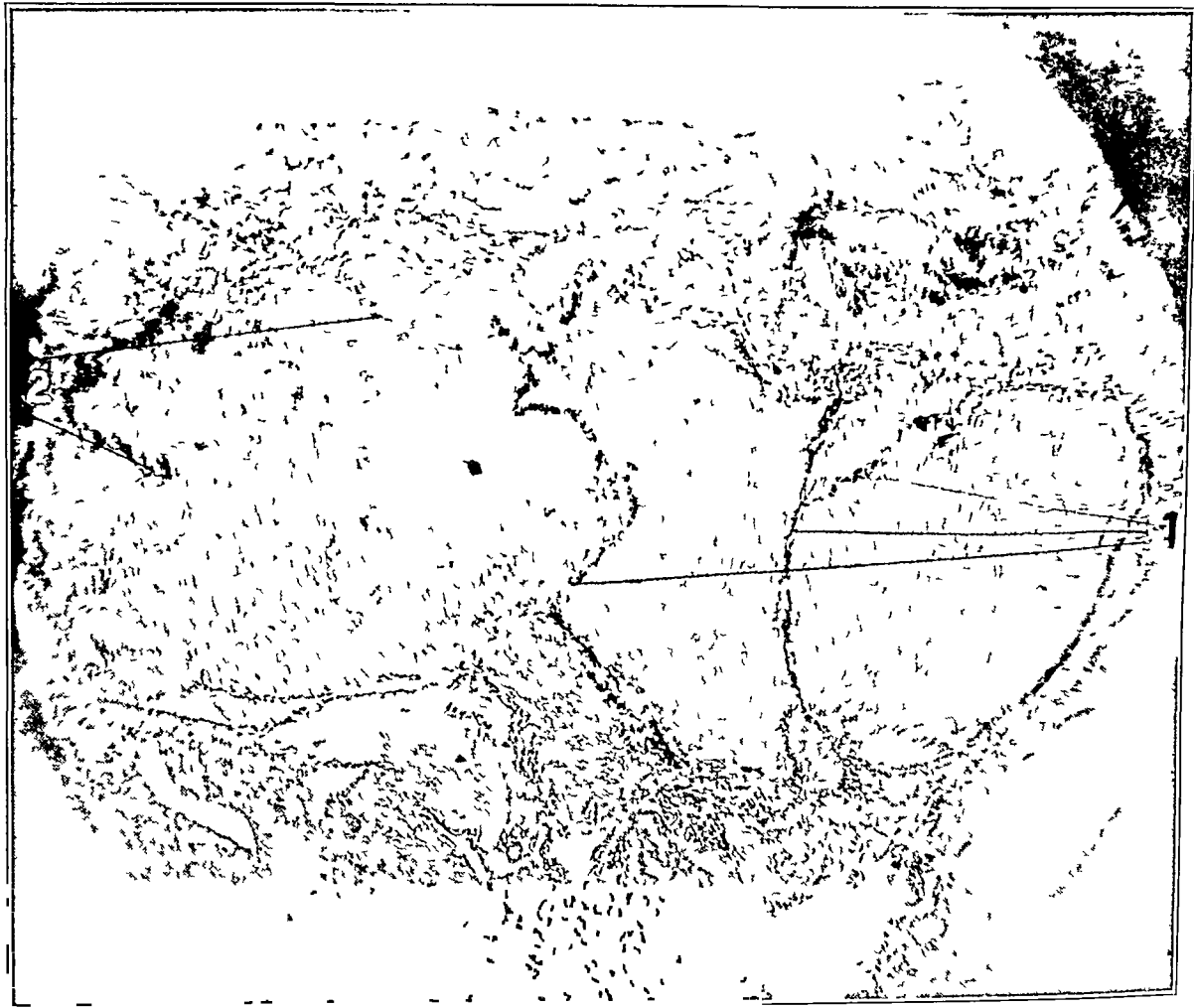


Fig 3 (case 4)—Higher magnification of figure 2. 1, thin walls separating the lacunae. These consist of two layers of endothelial cells separated by a thin layer of connective tissue, 2, incomplete bands of connective tissue projecting into the blood filled lacuna—the so-called angiomatic valves.

Urinalysis and a Wassermann reaction were negative.

*Operation*—On Sept 18, 1915, Dr McClure made an excision, using ether anesthesia. An incision was made over the tumor. When the biceps muscle was incised, the tumor was immediately evident as an angioma. It was multiloculated and soft, and was entirely limited to the short head of the biceps. The short head

was divided at its origin and the mass removed. There was little muscle tissue left in the short head. The muscle was cut across just above the cubital fossa. No large veins and no suggestion of communication with the brachial veins were seen. During the dissection the thin walls of the tumor were opened and dark blood escaped, causing complete collapse of the mass. Closure was made throughout with silk. The patient made an uneventful recovery.

*Gross Pathology*—The specimen consisted of a mass of tissue about the size of an egg. The tissue was red and was composed chiefly of muscle. On section, the cut surface was made up of a network of branching tubes, having the average diameter of a horse hair. These tubes were too small to demonstrate a lumen, but they were suggestive of blood vessels (Dr Webster).

*Microscopic Pathology*—Sections in this case did not show large spaces filled with blood although they were definitely demonstrated at operation. There were numerous blood vessels the walls of which showed thickening of the fibrous tissue or in other tissue of the intima. The muscle bundles were separated by masses of fibrous tissue and many muscle fibers were replaced by fat. Certain areas showed only connective tissue with irregular areas of smooth muscle. There was some small round cell infiltration in these fibrous areas.

*Subsequent History*—There was no recurrence after ten years.

*CASE 6—Diagnosis* *Intramuscular hemangioma of the biceps femoris, excision, recovery*

*Clinical History*—A white woman, aged 24, a nurse, an American, was admitted to the Johns Hopkins Hospital on Nov 7, 1918. The family history was unimportant. An appendectomy had been performed ten years before admission. After the operation for appendicitis, the patient noted a swelling of the posterior aspect of the right thigh. This was slightly annoying for two weeks but was never extremely painful. It had increased slightly in size. During the past two or three years the swelling had become tender on pressure, and she had been conscious of a tired dragging sensation in the right leg. After walking a short time, this sensation was not so noticeable.

*Physical Examination*—The results of the examination were negative except for the condition of the right thigh. There was a somewhat diffuse swelling at the upper part of the right popliteal space and extending upward from it. There were a few dilated vessels in the skin over the swelling. The skin was not adherent and was freely movable over the tumor. On palpation the tumor was soft, not tender, and seemed to extend between the biceps muscles. It was rather diffuse, and the edges were not definitely felt. It was slightly compressible. No thrill or bruit was present. Vertically, it measured about 10 cm and transversely about 6 cm. It projected out from the normal contour only to a slight degree. The results of a urinalysis were negative.

*Operation*—On Nov 8, 1918, Dr R. Follis made an excision using ether anesthesia. The patient was placed in the prone position and a vertical incision was made down the center of the right thigh over the tumor mass. As the deep fascia was incised, a diffuse reddish tumor was encountered beneath the sheath of the muscles without definite encapsulation. Inspection showed that the normal muscle fibers were continuous with the tumor itself. As attempts were made to circumscribe the tumor large venous sinuses were encountered and it became clear that the condition was one of intramuscular angioma. An effort was made to remove the growth cleanly with as little sacrifice of normal muscle as possible. Nowhere was it possible to shell out the tumor by blunt dissection. At the upper pole numerous bundles of muscle fibers running down into the tumor had to be cut.

The mass was then turned down and the lower attachment was cut. The severed ends of the muscle were sewed to the underlying hamstring muscles. The sciatic nerve was not seen during the operation. Closure was made with interrupted silk in the fascia, subcuticular silver wire was used in the skin. Bismuth gauze dressing and crinoline spica was used down the leg to the toes.

*Gross Pathology*—The tissue consisted of a tumor of the soft parts about the size and shape of a large goose egg. It was definitely circumscribed. On the section there were numerous blood vessels and sinuses, some patent and others filled with a gelatinous material. The muscles were bound together by tough fibrous tissue. Considerable muscle tissue was present.

*Microscopic Pathology*—The tissue was composed of loose fibrous bundles in which were many large spaces lined with endothelium. These spaces anastomosed with each other and were irregular in size and shape. Many were filled with blood. There were other blood spaces which did not seem to have any lining endothelium, and the blood seemed to be directly in contact with muscle or fibrous tissue. Many of these blood spaces had smooth muscle in their walls which seemed to bear a definite relationship to the wall. In a few areas there were partially organized thrombi. The fibrous tissue was short and wavy, and the cells were not numerous. In a few areas there were strands of smooth muscle. The striated muscle fibers were replaced in some parts by fat. In other areas they showed degenerative changes, being almost hyaline and without nuclei.

*Subsequent History*—The patient was reported to be well one year after the operation.

CASE 7—*Diagnosis* Intramuscular hemangioma of the gastrocnemius muscle and calf, partial excision, not improved.

*Clinical History*—A white girl, aged 14, a student, of Polish descent, had a personal and family history that was unimportant. In 1914, nine years before admission, the patient fell against a swing, injuring her leg. The leg was black and blue, and in a few days the condition cleared up. Two years later she began to limp, and the calf became enlarged. She was operated on, and a piece of tissue was removed and diagnosed fibroma. There was no improvement, and the child was taken to a second physician who advised tenotomy of the achilles tendon and examination of the tumor. The family refused to cooperate, and no further treatment was given until 1920, four years after the onset.

*Physical Examination*—The examination was negative except for the leg affected. The left thigh was smaller than the right. The hamstring muscles were contracted 15 degrees. There was a large, more or less symmetrical, tumor in the region of the calf muscles which was painful on pressure. There was a contraction of the achilles tendon and an elongation of all the extensor muscles of the dorsum of the foot.

Urinalysis and a Wassermann reaction were negative. The blood was normal.

*X-Ray Report*—Anteroposterior and lateral plates of the left leg showed a marked increase in both diameters of the calf. No involvement of the bone was noted except that there was a slight bowing of the tibia for a short distance at the junction of the upper and middle thirds. There were several irregular flecks in the calf muscles which were suggestive of myositis ossificans, but were probably phleboliths. A diagnosis of rhabdomyoma was made.

*Operation*—On Feb. 7, 1921, Dr. Hodgen performed an operation at the Blodgett Memorial Hospital. A tenotomy of the left achilles tendon was done, and a piece of the tumor was excised for examination. The tumor looked as if it were composed of fatty tissue, but it was so infiltrated with muscle that removal

was found to be impossible. The foot was put in good position, and a plaster cast was applied.

*Pathologic Report* (Dr. Warthin)—The piece of calf muscle showed no neoplasm. It presented the appearance of fatty atrophy of the striated muscle with angiomatous dilatation of the vessels and some local infiltration.

*Subsequent History*—After the cast was removed the foot was in good position, but there was still some contracture of the knee. Effort was made to have the child overcome this condition herself with the assistance of massage, but the attempt was not successful. The leg was then straightened under anesthesia and a plaster cast applied. The child suffered so much pain that the cast was removed after one month. The tumor was reduced. A brace was then fitted to the ankle but the knee was not confined.

For the following six months the child improved. She walked well although she always favored the left leg and sometimes complained of pain. The tumor was still about the same size. Radium was used without results. The mother reported that the child was again holding the leg stiff, and the contractures at the knee and the ankle were reappearing. Massage and stretching were tried, but these seemed to increase the difficulty and the leg was sensitive. Another x-ray picture showed a distinct increase in the size of the tumor. There was a distinct increase in the number and the size of the calcified flecks in the calf muscles.

The patient was shown to Dr. Bloodgood, who made the diagnosis of hemangioma of the muscle and advised further treatment. Bandages were applied, but the child cried because of great pain. Further operation was advised but no further report could be secured. The child was lost track of.

Case 7 shows clearly the difficulties encountered when these growths are not recognized and when radical measures are not used.

CASE 8—*Diagnosis Intramuscular hemangioma of the masseter muscle, excision, recovery*

*Clinical History*—A white man, aged 29, a coal miner, an Italian, was admitted to the Union Memorial Hospital on Dec. 18, 1922. The family and past histories were negative. Six years before admission, while in the Italian army, the patient was wounded in the right jaw by shrapnel. The wound was treated in a base hospital for several weeks. On discharge from the hospital, the patient noted a lump over the angle of the right jaw. This had not increased in size and had never given him any trouble until one month before admission when he began to have pain. The pain was in the swelling and varied in duration from a few moments to half a day. He went to the Johns Hopkins Hospital where operation was advised and x-ray photographs were taken.

*Physical Examination*—The results were negative, except for the condition of the right cheek. There was a swelling about the size of a walnut in the region of the angle of the right mandible. The skin over the swelling was normal. The tumor was soft on palpation. Buried in it were several hard nodules about the size of the head of a black pin. The swelling was freely movable and did not seem to be attached to the skin or bone. There was no impairment of function. The results of a urinalysis were negative.

*X-ray Diagnosis*—The original report stated that there was shrapnel in the cheek, and the characteristic appearance of the phleboliths was missed. The plate was secured for this study and showed a piece of shrapnel and three phleboliths. The phleboliths were oval and showed characteristic concentric rings. This type of shadow could not be made by iron. The bit of shrapnel was in another part of the head far from the tumor (fig. 4).



*Operation*—On Dec 20, 1922, an operation was performed under gas and ether anesthesia by Dr J M I Finney, Jr. An incision was made along the inferior ramus of the right jaw from the angle anteriorly for about 3 inches (7.6 cm). The dissection was then carried upward over the cheek until the tumor was seen and delivered into the wound. The tumor seemed to be composed completely of blood vessels, and much hemorrhage was encountered. Six calcareous nodules were removed, varying in size from that of a black pinhead to that of a pea. The

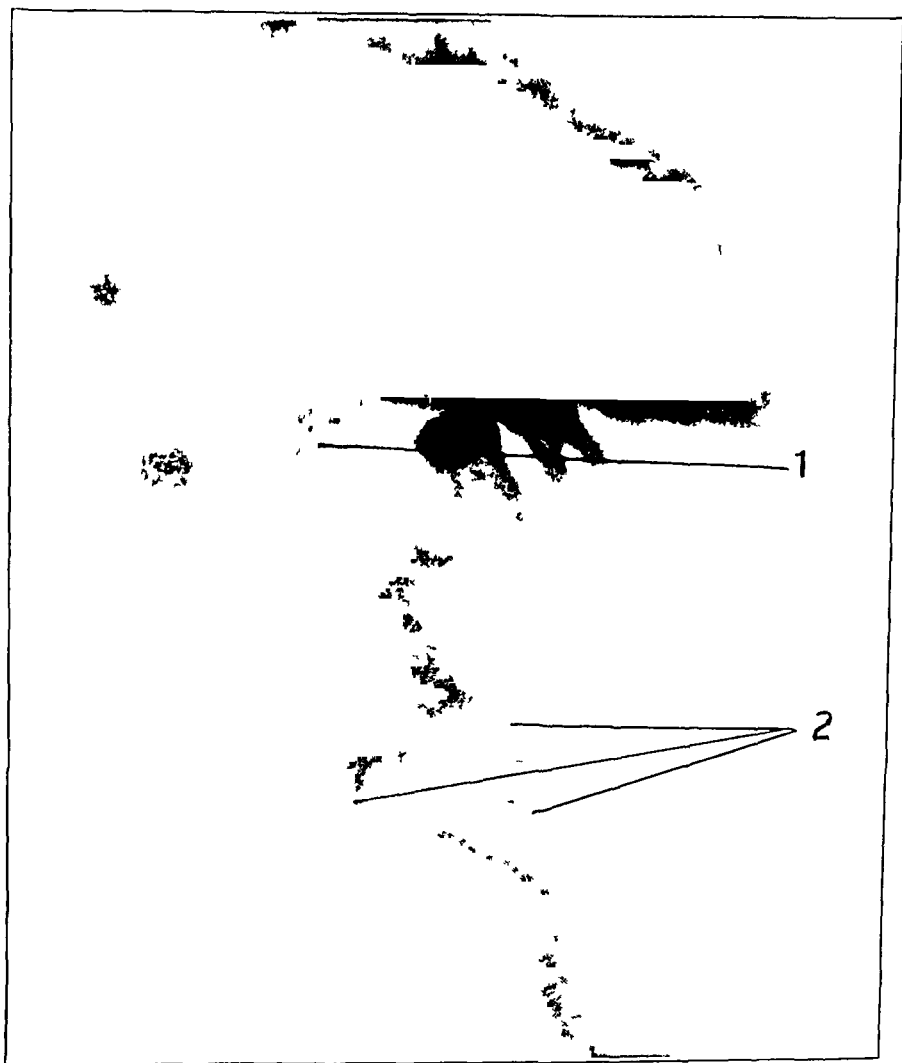


Fig 4 (case 8)—1, shrapnel, 2, phleboliths. The shadows cast by the phleboliths are oval and show concentric rings. The operator reported that he removed six stones, but in the picture only three are seen. No shrapnel was located in the tumor.

tumor was freed with considerable difficulty and was dissected up from the masseter muscle. More exposure was necessary and a second incision was made at right angles to the first, which extended for 2 inches (5 cm) down the neck. The facial nerve was seen. The tumor was then completely excised, and closure was made with fine silk. A small protective drain was placed at the intersection

of the two incisions. The drain was removed entirely on the fourth postoperative day. The patient made an uneventful recovery.

*Microscopic Pathology*—There was a large amount of cellular fibrous tissue which separated the bundles of striated muscle. Some of the muscle bundles showed hyaline degeneration, and in some areas fat had replaced the muscle fibers. There were a few endothelial lined blood spaces, but most of them seemed to lack endothelium, and the blood was bounded by the fibrous tissue. In this case the blood vessels showed a thickening of the intima. In some vessels the intima was three or four times as thick as the wall of the vessel and the lumen was extremely small. There was no cellular infiltration.

The patient left the hospital in good condition, and no further record has been secured.

*CASE 9—Diagnosis Intramuscular hemangioma of the splenius capitis and semispinalis capitis, excision, recovery*

*Clinical History*—A white man, aged 33, an engineer, an American, was admitted to the Union Memorial Hospital on March 13, 1923. The family history was negative. Appendectomy with drainage had been performed in 1913, tonsillectomy was done in 1918. Tuberculosis was suspected in 1918. In 1914, nine years before admission, after raising a window on a train, he felt a sudden pain in the right side of the neck, and on investigation found a soft tender lump about the size of the end of a finger. There had been a large mass on the right shoulder for some years which the patient attributed to carrying a heavy transit on the shoulder. The soreness disappeared in a few days, and the patient was not troubled with the lump, which persisted. He was examined by various physicians who made light of the condition. A year before examination, the lump began to enlarge and become painful. Under the diagnosis of lipoma it was operated on five months before admission. A bloody tumor was found running under the clavicle, and the surgeon believed he had removed all of it. About six weeks later the patient noted that the lump began to return. It became swollen when he was lying down and smaller during the day when he was up. There was aching and tenderness in the tumor when it was swollen. It did not pulsate. It had been getting worse steadily, and at times became as large as a hen's egg. Following the operation there was a paralysis of some of the muscles of the shoulder. The use of the shoulder and arm had come back almost entirely, but there was persistent pain under the right scapula.

*Physical Examination*—On the left upper part of the chest and extending down the left arm to the thumb and first two fingers of the left hand, there was a reddish-brown birthmark, following exactly the course of the median nerve. The birthmark appeared as a group of small papillary purpuric spots. The color could not be pressed out of it. The patient said that it changed color rapidly, becoming purple when he was chilled or when emotionally wrought up.

On the right side of the neck there was a scar about 4 inches (10.16 cm) long with a slight tendency to keloid formation. In the upper half of this scar a swelling was seen, which was about the size of the end of the thumb. It was soft and not tender. At about the center was a small hard nodule which was tender. There was no pulsation, no thrill and no bruit. It could not be reduced by pressure. It was situated in the posterior angle, and nearly over it there was a grayish-blue area of skin about the size of a thumb nail. During examination the tumor suddenly became twice its size and then subsided. It seemed to extend upward and posteriorly, disappearing under the trapezius and the deeper muscles of the neck. There was a definite fulness under the posterior pharyngeal wall on the right side which corresponded to the level at which the tumor disappeared under the muscles.

of the neck. Urinalysis was negative. The condition was diagnosed as a thick-walled cyst.

*Operation*—On March 17, 1923, Dr. J. M. T. Finney made an excision, using ether anesthesia. The old scar which ran along the outer border of the trapezius muscle on the right side was excised, and the sternocleidomastoid muscle was exposed and retracted anteriorly. The trapezius muscle was retracted posteriorly, which exposed the spinal accessory nerve. The tumor was now seen just under the trapezius and seemed to be in the belly of the splenius capitis and the semispinalis capitis muscles. It seemed to be angiomatous, and several small concretions could be felt in it. In attempting to dissect the tumor out, it was opened and a considerable amount of blood escaped. The splenius capitis and the semispinalis capitis were cut across well above and below the tumor, and this section of the muscles was removed. All bleeding points were ligated. The tumor was about the size of a large walnut. An attempt was then made to establish a connection between this tumor and the bulging in the posterior pharyngeal wall on the left side, but no connection could be made out. The wound was closed. The patient made an uneventful recovery.

*Gross Pathology*—The specimen consisted of fat and muscle filled with hemorrhage. The polychrome methylene blue (methylenium chloride, U.S.P.) frozen section did not show evidence of a malignant condition (Dr. Bloodgood).

*Microscopic Pathology*—The tissue consisted of muscle, fat, fibrous tissue, blood vessels and blood spaces. Some of the blood spaces were lined with endothelium, others were not. They were all irregular in size and shape. Some of the blood spaces rested against muscle which showed atrophic changes. One area of blood was partially organized. The blood vessels had thickened walls. In some the intima was thicker, in others the fibrous tissue was increased. The fibrous stroma was extremely cellular. There were a few minute blood vessels in this fibrous tissue which was wavy. Fat had replaced muscle in some places, and the blood spaces rested against it. The whole picture was one of blood vessels and blood spaces in fat and muscle. There was a large amount of blood pigment throughout.

The patient was discharged cured. No further report was obtained.

*CASE 10—Diagnosis: Intramuscular hemangioma of the soleus muscle, excision, recovery.*

*Clinical History*—A white girl, aged 13, a school girl, an American, was admitted to the Union Memorial Hospital on June 17, 1928. The past and family histories were negative. Six years before admission, at the age of 7, while posing on her toes at a dancing class, she felt a sudden severe pain in the medial aspect of the left calf. The pain became less severe in a few minutes, and she continued dancing until the lesson was finished. In a few days the pain entirely subsided. Since that time there had been tenderness but no pain except when the area was palpated. Two years before admission, the parents noted that the left calf was smaller and that the child was gradually beginning to limp and complain of weakness in the leg. However, she indulged in athletics without any limitation of motion. The condition was diagnosed as hip disease and rheumatism, and various treatments were given without results.

*Physical Examination*—The results were negative except for the condition of the left leg. The left leg was symmetrically smaller than the right in circumference. There was a difference of 4 inches (10.16 cm.) in circumference in the calves and 4 inches in the mid thigh. There was no shortening of the leg. There was some tenderness in the calf but no swelling. Some induration was palpable.

in the calf, and some weakness was noted on dorsiflexion of the foot. No other limitation of motion was found. The diagnosis was myositis. The results of a roentgen examination, urinalysis and a Wassermann test were negative.

*Operation*—In June, 1928, Dr. Baer made an operation, using ether anesthesia. An incision was made over the middle of the upper portion of the left leg beginning below the knee joint over the calf. The gastrocnemius muscle was exposed and divided, exposing the soleus muscle. A nodular swelling was found in the belly of the soleus muscle about 2 inches (5 cm.) long and 1 inch (2.5 cm.) wide. It was recognized as an angioma, and excision was attempted. There was a great deal of bleeding which was hard to check. The muscle was cut almost through below and the tumor mass was gradually removed (fig. 5). The patient became shocked from hemorrhage, and a subpectoral infusion of physiologic solution of



Fig. 5 (case 10)—Photograph taken during the operation. 1 the gastrocnemius is shown retracted above. 2 the tumor mass is seen drawn down by a clamp. The nodular appearance can be made out which is due to cavernous spaces protruding out of the muscle. 3 the remainder of the soleus is seen from which the tumor mass has been partially dissected.

sodium chloride was given. The wound was packed with iodoform gauze. The gastrocnemius muscle was sutured with catgut. The skin was partly closed with silk and a plaster cast was applied. The gauze was removed after nine days. The recovery was uneventful.

*Gross Pathology*—The specimen was about 3 inches (7.6 cm.) long and 2 inches (5 cm.) wide. It was red with bluish nodules on the surface. It had the consistency of muscle while the small nodules felt cystic. Figure 6 shows the nodular appearance of the surface of the growth. On section it had the appearance of a sponge. There were many small tubes filled with blood among the muscle fibers. There was no fat. One could not make out whether the blood filled tubes were vessels or lacunae.

*Microscopic Pathology*—Sections showed the typical picture of angioma. There were lacunae of different shapes and sizes filled with normal blood. Some were lined with endothelium, while others appeared to have walls of connective tissue without any lining (figs 7 and 8). The connective tissue was loose and had scant

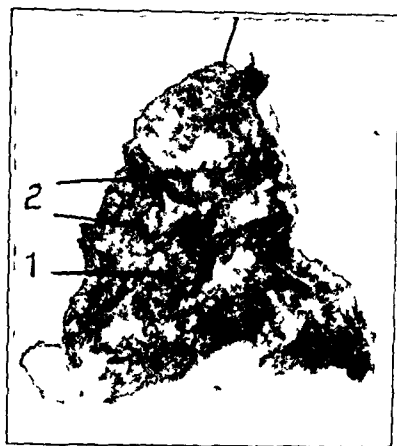


Fig 6 (case 10)—1, muscle, 2, nodules of angioma penetrating the muscle tissue. These nodules looked like varicose veins and were bluish against the dark red of the muscle tissue.

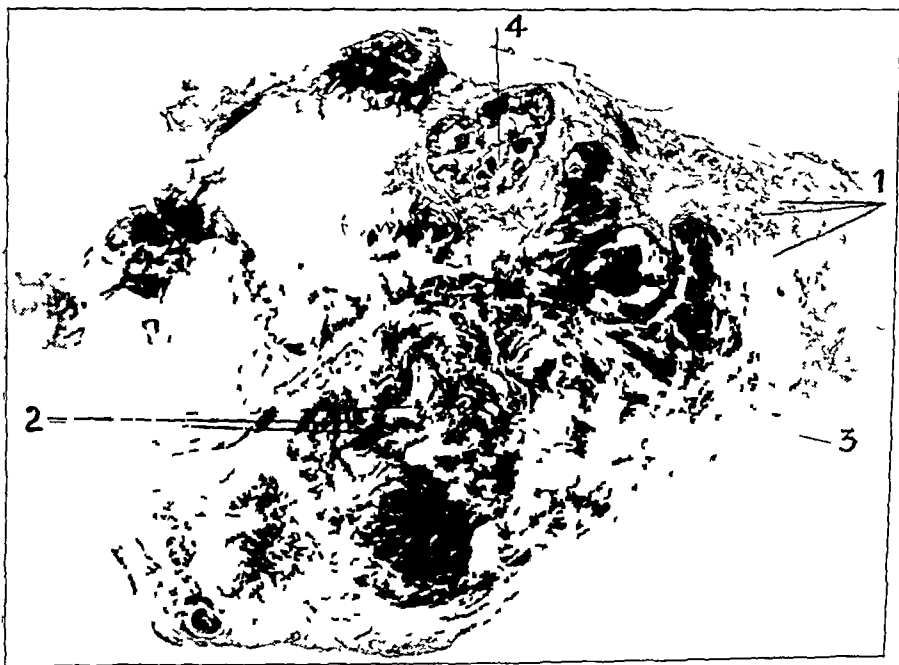


Fig 7 (case 10)—1, shows the infiltration of the angioma into the muscle. Many small blood vessels are present throughout the entire section, 2, near the center are three large vessels which have a definite increase of fibrous tissue in the walls, 3, in the center of the section is an area which consists of connective tissue enclosing normal blood, 4, the upper space shows partitions of connective tissue in the lacuna.

cells. Muscle fibers showed atrophy, but no fat was seen in this specimen. Some of the vessels had a thickened intima. A number appeared to have no lumina, being filled with the endothelial cells. There were some fibers of smooth muscle in the connective tissue arranged around the lacunae. There were no areas of round cell infiltration.

CASE 11—*Diagnosis* Intramuscular hemangioma of the serratus magnus  
excision, recovery

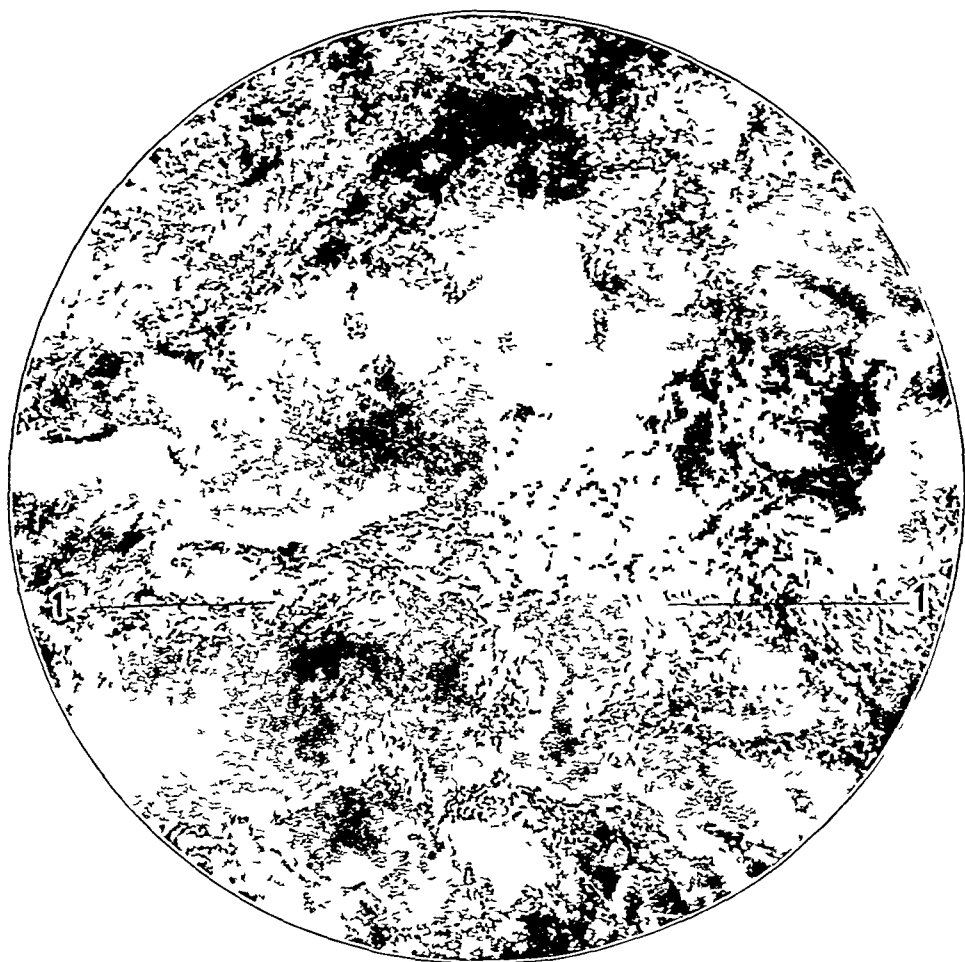


Fig 8 (case 10)—A higher magnification of the center of figure 7 1, the loose connective tissue is seen enclosing the normal blood. There was no endothelial lining in these areas.

*Clinical History*—A white woman, aged 26, a housewife, was admitted to the Union Memorial Hospital on Sept 6, 1928. The family and past histories were negative. Three years before admission she accidentally discovered a swelling below the left scapula. This occurred shortly after she had been vaccinated and she consulted her physician who said that it was unimportant. The swelling gradually became painful and increased in size. The pain would last for a few

days and then subside. While the pain was present, the swelling would feel tense and hot. Counter irritants were applied which did not help. The swelling would become less tense after a few days and the pain would disappear. This continued for three months, gradually becoming more frequent, and the patient consulted a surgeon, who diagnosed the condition as lipoma and tried to excise the mass under local anesthesia. He encountered profuse bleeding and packed the wound telling her that it was a tumor of the blood vessel and that after the incision had healed she should go to the hospital and have the mass excised. The pack was removed in four days and the wound healed. She had no further pain, so she did not seek further treatment until one month before admission. The pain began to reappear and the intervals between the attacks of pain became shorter so that she had pain almost continuously. She consulted a surgeon in Virginia, who made a diagnosis of lipoma and advised removal. In the meantime, she came to Baltimore, and as the pain continued to annoy her, she applied for treatment.

*Physical Examination*—The results were negative, except for a slight bilateral enlargement of the thyroid gland. On the back just under the lower border of the left scapula was a scar about 2 inches (5 cm) long. Beneath this scar there was a firm movable mass the borders of which were not distinctly made out. It was not adherent to the skin and was nonpulsating. The mass was about 8 cm across and was not painful to palpation. She said that after prolonged pressure, as after lying on it, the mass became tender to touch.

Urinalysis was negative. The diagnosis was lipoma.

*Operation*—On Sept 7, 1928, Dr T. Otto made an excision, using ether anesthesia. The old scar was excised. As the tumor was being exposed, it was recognized as an angioma of the serratus muscle. The serratus was then cut across below and the tumor dissected up. Large veins were found in the upper end which were cut across and ligated with catgut. The muscle was cut across above and the tumor removed. Closure was made with catgut and silk. Two rubber drains were placed and dry dressing applied.

*Gross Pathology*—The specimen consisted of a piece of muscle and fat. The muscle was fan-shaped, being  $1\frac{1}{2}$  (3.77 cm) inches across at the top and 3 inches (7.5 cm) across at the lower end. It was 4 inches (10.16 cm) long and  $\frac{1}{2}$  inch (1.27 cm) thick. The striations of the muscle could be seen through the muscle sheath (fig 9). On palpation a hard nodule, about the size of a lead shot, was felt in the lower end. The fascia was carefully removed and was found to be adherent to the lower end of the specimen. Here blood vessels were seen which had penetrated the muscle. The nodule was found to be half embedded in the muscle, and the fascia was removed from its surface (fig 10). A second smaller nodule was then palpated deeper in the muscle and nearer the center of the specimen. On section the muscle was found to be infiltrated by channels containing blood, looking very much like a sponge filled with clotted blood. Most of the channels were irregular in shape and size while a few were circular and looked like blood vessels. The large nodule was found embedded in fibrous tissue. The smaller nodule was found in one of the blood filled channels (fig 11). A roentgenogram of the specimen was made, and three shadows were seen. These were oval and showed concentric rings (fig 12).

*Microscopic Pathology*—Sections showed cavernous spaces, which were irregular in size and shape. Some were filled with normal blood and some were filled with a pale eosin-staining material which was laked blood. These spaces were separated from each other by cellular fibrous tissue which was wavy. Some of the spaces were lined with endothelium, others did not have any lining at all, the blood

being in contact with the fibrous tissue. Here and there were bundles of striated muscle lying in the fibrous tissue or in a cavernous space and being completely surrounded by blood. There were areas in which fat had replaced some of the muscle fibers in a muscle bundle. No smooth muscle was seen in the sections. There were a few large blood vessels which appeared to have normal walls and except for their size would be normal.

*Subsequent History*—On discharge, the patient did not complain of any pain and had no impairment of function.

#### SUMMARY OF ELEVEN HITHERTO UNREPORTED CASES

Ten cases occurred in white persons and one in a negro. This is the only case on record as far as we could find of a primary angioma of striated muscle occurring in a colored person. Five occurred in males and six in females. The ages at which the patients applied for treatment ranged from 12 to 69. Three were in the second decade, five in the

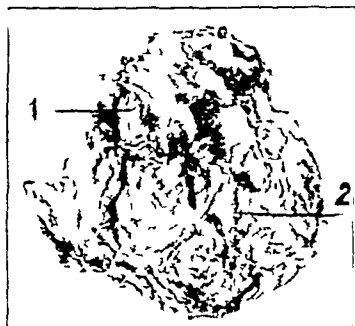


Figure 9

Fig 9 (case 11)—Gross specimen. 1, striations of muscle, 2, fascia covering muscle.

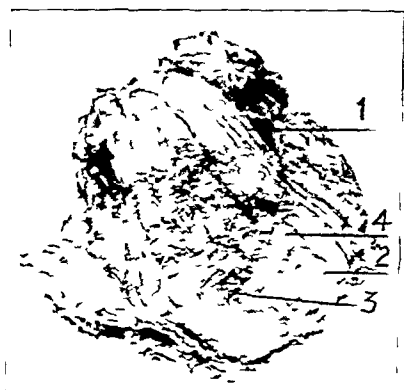


Figure 10

Fig 10 (case 11)—1, striations of muscle, 2, phlebolith imbedded in muscle, 3, cavernous angioma penetrating muscle into fascia, 4, fascia adherent to muscle.

third decade, two in the fourth decade and one in the seventh decade. It is interesting to note that almost half came for treatment in the third decade, that is, in the twenties. Furthermore, eight came for treatment before the fourth decade. If the age of onset of symptoms is analyzed, one finds that five began in the first decade, one in the second, four in the third and one in the seventh. We find, therefore, that although no patients applied for treatment before the age of 11, five were already aware of the presence of the tumor. A history of trauma was given in five cases, and no history of trauma in six cases. The chief symptoms were given as swelling, pain and impairment of function. In all the cases there was a record of swelling or tumor formation. A history of pain was reported in nine cases, there was no pain in two cases. This



is the symptom which caused most of the patients to apply for treatment. In two cases, pain was the first symptom even before a swelling was noted. Function was impaired in four cases. In two of these cases the impairment of function was due to pain, while in the other two the tumor had caused contractures and deformities.

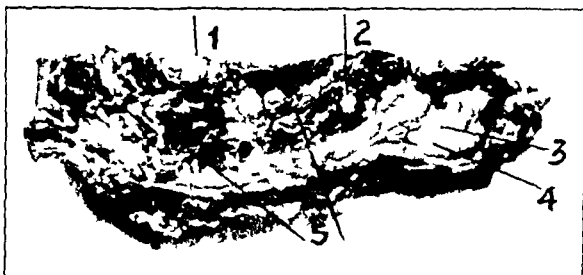


Fig 11 (case 11) —1 phlebolith embedded in fibrous tissue, 2, phlebolith in a cavernous space, 3, fat which has replaced muscle, 4, muscle tissue, 5, cavernous spaces of the tumor

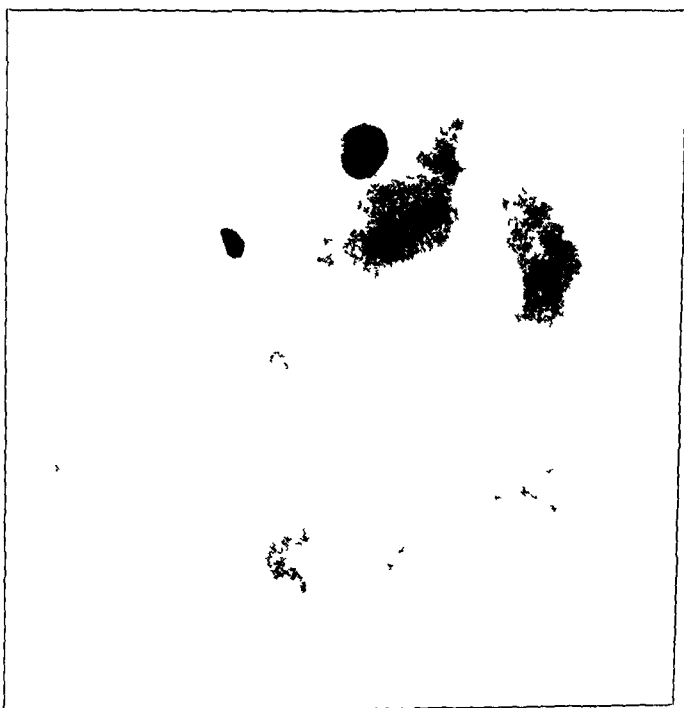


Fig 12 (case 11) —X-ray picture of the specimen. The oval shadows are thrown by the three phleboliths. The concentric rings are distinctly seen in the largest shadow.

Phleboliths were found in four cases, however, in two of these they were not found until examination of the pathologic specimens after operation. In none of the cases reported was a diagnosis made because of their presence.

A correct preoperative diagnosis was made in two cases. In three of the remaining nine cases a diagnosis of lipoma was made—a common error in diagnosis of these tumors. The other diagnoses were malignant ulcer, clubfoot of cerebral origin, ganglion, rhabdomyoma, cystic tumor and myositis.

The location of these tumors was as follows: five in the lower extremities, two in the upper extremities, two in the muscles of the head and one each in the muscles of the neck and trunk. Nine of the tumors were found in large muscles. The masseter muscle was involved twice and the gastrocnemius twice. The soleus, biceps brachii, triceps femoris, serratus magnus and adductor longus are some of the other large muscles that were involved by these tumors.

The tumor was excised in nine cases. A biopsy was done in one of the other cases and on the last one an amputation was performed after an excision.

TABLE 2—*Classification of Cases According to Age\**

Decade	Treatment Applied For	Symptom First Appeared
1	30	51
2	62	52
3	49	25
4	14	3
5	6	3
6	1	0
7	3	1
Total	165	165

\* No age was recorded in forty-seven cases.

Ten patients were reported well and one improved. The one that was reported as improved was the case in which a biopsy was done to try to determine the diagnosis, and further treatment was not carried out because of lack of cooperation.

This small series of cases runs true to the results found in larger series as will be seen later in this study.

#### SUMMARY OF TWO HUNDRED AND TWELVE CASES

The following is a summary of the 212 cases collected in this report.

*Age*—In table 2 we have classified the cases according to the age at which the patients applied for treatment and the age at which the symptoms first appeared. The ages have been divided into decades for convenience.

Of the 165 cases in which the age of onset was recorded, eighty-one or a little less than half showed symptoms before the eleventh year; 133, or less than three-fourths, before the twenty-fifth year, and all but seven before the thirty-first year. It is also interesting to note that whereas eighty-one gave symptoms before the end of the tenth year, only

thirty applied for treatment in that decade, the rest applying later. The majority, or 111, applied for treatment between the ages of 11 and 30.

The symptoms appeared before the third decade in 133 cases, indicating that this growth is most common in early life. There were twenty-five cases in the third decade and the remaining seven occurred after the age of 30. Most writers up to the present time have stated that primary angiomas of the muscle occur chiefly between the ages of 15 and 30. These statements are incorrect as the foregoing figures indicate. The majority of these tumors appear before the age of 20. This observation may be of some value in making a diagnosis.

*Sex and Race*—The cases are about equally divided between the sexes as table 3 shows.

All the cases with the exception of seven occurred in the white race. Six reported by Nagatomi were among the Japanese, and one patient in our series was colored. It is impossible to point out any geographic distribution, although the literature shows most of the cases reported from Italy, France and Germany. More interest has probably been taken in this class of tumors in those countries and therefore more cases reported.

TABLE 3—*Sex Incidence*

Male	Female	Not Recorded
79	84	49

Personal history, social condition, occupation and dietary influence add nothing of importance to the etiology.

Heredity plays no part in the etiology of these growths. Transmission of primary angioma of the muscle from parents to children, or the occurrence of this tumor in two children of the same family, has never been recorded.

*Symptoms and Diagnosis*—The chief symptoms are pain, swelling and impairment of function. There was pain in 100 of the 123 patients definitely reporting on the presence or absence of pain. There was no swelling or tumor in only three cases, function was impaired in forty-seven cases.

The diagnosis is extremely difficult. The correct diagnosis was made in only eighteen of the 212 cases tabulated. This is probably due to the inaccessibility of this type of tumor.

*Site*—The location of these tumors was found to be as shown in table 4. On further subdivision we find that the seventeen cases involving muscles of the head, the masseter was involved alone in nine cases, with the buccinator in one case. The muscles of the eyes were involved in three cases and the temporal muscle and the muscles of the tongue in two cases each. All questionable cases of the tongue were eliminated.

Of the muscles of the trunk the latissimus and the trapezius were involved in twenty cases the remaining thirty-seven being distributed among all the other muscles. In the upper extremity fifteen cases were in the arm twenty in the forearm and ten in the hand. It is interesting to note that of the fifteen cases occurring in the arm the triceps was involved alone in eight and with other muscles in two cases the biceps was involved alone in the remaining five cases. In the lower extremity fifty-two were in the thigh forty in the leg and ten in the foot. The quadriceps femoris and the vastus internus were involved in sixteen cases each making thirty-two of the fifty-two cases. The gastrocnemius was reported alone in ten and with other muscles in eight cases accounting for eighteen of the forty cases.

TABLE 4—Location of Tumors

	Cases
Muscles of head	17
Muscles of trunk	57
Muscle of upper extremity	45
Muscles of lower extremity	92
Muscle not given	1

TABLE 5—Treatment Employed and Results Obtained

	Case
Total excision and recovery	137
Total excision with no statement of outcome	5
Partial excision with recovery	7
Partial excision repeated for recurrence and recovery	3
Partial excision with later amputation	2
Amputation and recovery	5
Electrolysis and improvement	1
Cauterization and improvement	2
Biopsy and no improvement	1
Treatment not stated	29

The lower extremity, therefore, is the chief site of these tumors. We further noted that the large and powerful muscles were most commonly affected. The masseter, latissimus dorsi trapezius, triceps brachialis, biceps brachialis, quadriceps femoris, vastus internus and gastrocnemius accounted for ninety-five cases. No doubt motion plays a big role in the growth of the tumor, and the impairment of motion in any of these larger and more important muscles is of vital importance to the patient. Perhaps that is the reason why these patients came for treatment while many others in less important muscles were not troublesome and so were passed unnoted by the patient.

*Treatment and Result*—Table 5 shows the type of treatment employed and the results obtained. It is evident that excision of the growth is sufficient to insure a cure providing the excision is complete.

## CONCLUSION

Primary angiomas of striated muscles are no longer rare tumors, as is indicated by the 212 cases here collected. It is a slow growing tumor, congenital in origin with trauma playing a role more in its growth than in its origin. It occurs about equally in both sexes. The age of onset is before the twenty-first year in the great majority of cases, the largest number occurring before the eleventh year. They may occur in any striated muscle. The lower extremities are most commonly affected and the upper extremities are next. The large and more powerful muscles are involved most frequently. The size of these tumors ranges from that of a nut to that of a small pumpkin. The muscle involved plays a passive rôle. The chief symptoms are pain, swelling and functional impairment, although any one or all may be lacking. The skin is usually normal. The tumor may be compressible and change in size with changes in posture. It is usually soft but may be hard, smooth or lobulated, movable or fixed, circumscribed or diffuse. The diagnosis is difficult. Aspiration of normal blood is a valuable aid. The x-ray pictures may be of assistance when phleboliths are present. The existence of simple angiomas is questioned, and the cavernous type is considered the only one found in striated muscle. On section it has the characteristic appearance of a blood filled sponge. There is no particular afferent or efferent vessel. Microscopically, the typical picture is that of blood filled spaces, containing normal blood, which either are lined by endothelium or have walls composed of fibrous connective tissue. Some smooth muscle is seen in the connective tissue. The vessels may have a thickening of the intima or of the adventitia. The muscle fibers show degeneration ranging from hyaline to fat replacement. The only treatment of value is excision. The prognosis is excellent.

# OPERATIVE SURGERY OF THE HIP JOINT

ASTLEY P. C. ASHHURST, M.D.

PHILADELPHIA

My personal experience in the operative surgery of the hip joint extends over more than twenty years and comprises more than 100 operations, these are summarized in table 1. Of these, eighty-six were in the nature of reparative or reconstructive operations while only seventeen can be classed as destructive, such as those listed as "excision" for acute osteomyelitis or for tuberculosis with secondary infection. I have omitted amputations at the hip joint.

TABLE 1—Summary of Operations (to April 1, 1929)

Operation	Cases	Deaths
Arthrodesis	6	0
Arthroplasty	8	0
Bone peg	2	0
Bone implants	1	0
Capsulorrhaphy	3	0
Excision	17	2
Open reduction	13	1
Osteoclasis (Anzoletti)	2	0
Osteotomy	15	1
Reconstruction	27	1
Transfer of tensor fasciae	6	0
	103	5

It is my purpose to discuss (1) the indications for the various operative procedures, (2) the technic of the operations and (3) the results.

## INDICATIONS FOR THE VARIOUS OPERATIVE PROCEDURES

*Arthrodesis*—Arthrodesis is the operative production of ankylosis in the effort to improve function. Its main indication is found in cases of flail-joint due to anterior poliomyelitis. Fortunately there are not many patients in whom residual paralysis leaves one or both hips in a flail-like condition and even under these rare circumstances it is necessary that the patient's spinal and abdominal muscles be sufficiently strong to be able to control the lower extremity through the pelvis after the femur has been fixed to the latter. It would be as useless to produce ankylosis between the femur and the pelvis when the latter could not

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\* From the Episcopal Hospital and the Philadelphia Orthopaedic Hospital.

\* Read at a Meeting of the International Society of Surgery, Warsaw, Poland, July 24, 1929.

be controlled by the patient as to do arthrodesis of the shoulder when the muscles running from the trunk to the scapula were powerless to move the latter

Arthrodesis of the hip has also been recommended to abolish pain in cases of hypertrophic arthritis. I have adopted it only once in such a case, and I believe that the modern reconstruction operation is more efficient. I attempted once also to produce ankylosis in a case of neuro-pathic arthritis (Charcot joint) at the hip, but without success, I doubt whether any operation on a Charcot hip is advisable

*Arthroplasty*—By arthroplasty is implied an operation designed (by means of the interposition of soft tissues between the bone ends) to restore motion to a joint which is ankylosed. When applied to the hip joint (Nelaton) it is necessary, in my opinion, for the surgeon to convince himself concerning the following points: 1 The patient is sufficiently incommoded by the ankylosis which is present to justify a serious operation which does not always ensure both free motion and stability, in other words, the operation may result in too great mobility with instability, or it may result in recurrence of ankylosis. 2 The ankylosis is not due to pyogenic organisms or to tuberculosis, since such an operation in such a case may rouse dormant infection and hence fail to improve the patient's condition. 3 Approximately the normal form of the head and neck of the femur has been preserved, in other words, ankylosis has developed without destruction of bone

From the foregoing paragraph it will be seen that I regard the indications for a typical arthroplasty as extremely limited, indeed, since the better development of the technic of "reconstruction of the hip," as improved by Whitman, Gill and others, the indications for typical arthroplasty have almost disappeared. I have seen no patient since 1920 in whom I thought it could be employed with advantage. I have adopted the typical operation, much as described by John B. Murphy, only eight times: twice for pathologic dislocation (for which the reconstruction operation is undoubtedly better) and six times for bony ankylosis. In four of the six cases of bony ankylosis the postulates enumerated were present—two cases of bony ankylosis following gonococcic arthritis and two cases following arthritis from unknown metastatic infection almost certainly not pyogenic. In cases of ankylosis due to pyogenic infection such as healed osteomyelitis, I believe that a formal arthroplasty is too apt to stir up the old disease and that for such cases even if there has been little destruction of bone as well as for cases of pathologic dislocation, the operation of reconstruction is safer and gives better results.

*Bone Peg*—For ununited fracture of the neck of the femur the bone peg method of fixation is inferior, I believe, to the typical reconstruction operation of Whitman. I have employed it only five times,

and have not always found it easy to place the bone peg in the correct axis of the neck and head of the femur so as to fix both fragments. For the last ten years I have abandoned this operation.

*Bone Implants*—I have included in table 1 one operation for extensive fibrocystic disease of the trochanteric region and neck of the femur in which I placed massive transplants from the tibia into the cavity left by clearing out the diseased tissue.

*Capsulorrhaphy*—In three cases of recurrent paralytic dislocation of the hip due to anterior poliomyelitis I secured complete relief from the disability by opening and overlapping the distended capsule, dressing the limb in plaster of paris in the abducted position. The patients were 5, 11 and 17 years of age respectively at the date of operation. By the use of proper after-treatment (apparatus gymnastics) the muscles the weakness of which formerly permitted recurrence of the dislocation developed sufficiently to secure good stability and to maintain reduction. All the dislocations were upward and backward. In hips which are entirely flail and which are suited therefore for arthrodesis, there are no muscles strong enough to produce dislocation. The occurrence of paralytic dislocation requires complete or almost complete paralysis of the gluteus medius, with the hip held in flexion, adduction and internal rotation by the nearly or entirely intact antagonists.

*Excision*—More or less of the upper end of the femur and sometimes also portions of the acetabulum are removed. As already indicated, this is, strictly speaking, a destructive operation although it is done in the effort to save the patient's life by disinfection of the joint in cases of (1) acute osteomyelitis which has invaded it, (2) in cases of tuberculosis of the joint with secondary infection in children, or (3) even in early stages of tuberculosis of the hip joint in adults. I have also employed it in a few cases of nonunion as advised by Lambotte.

*Open Reduction*—Open reduction is applicable to congenital dislocations in those patients (1) in whom closed reduction and proper maintenance have eventually given rise to recurrence of the dislocation or (2) in whom reduction by the closed method proves impossible. When open reduction is possible without undue trauma, it is possible to prevent its recurrence by a plan originally suggested by Albee which consists in turning down, above the acetabulum, a roof of bone which deepens the cavity; this method has been employed by Lance, Ombredanne and others and has been systematized and popularized by my former assistant and present colleague, Prof. A. Bruce Gill. As Gill pointed out, congenital dislocations fall into three types: (1) the subluxation type in which the head is too large for the acetabulum and in which recurrent but easily reducible luxation may occur; (2) cases of complete dislocation reducible only by the open method but without the use of



great force, and (3) cases in almost all patients over 10 years of age in whom even with open operation it usually proves impossible, or possible only by unjustifiable force, to replace the head in the acetabulum. For the patients in the first and second categories, open reduction is an excellent operation, especially when Gill's roof of bone is made, but for most patients over 10 years of age persistence in attempts at reduction not only may entail severe shock,<sup>1</sup> but even if reduction is secured and maintained, the hip is apt to become the seat of ankylosis in bad position, this position having been adopted at the time of operation because the most stable position for maintenance of reduction. Hence for the latter patients the operation of reconstruction is preferable, and I have lately abandoned open reduction for any but patients in the first and second classes.

*Osteoclasis* (Anzoletti).—The method of osteoclasis described by Anzoletti consists (1) in inducing rarefaction of bone and absorption of its salts by keeping the parts immobilized in closely fitting gypsum

TABLE 2—Conditions in Which Osteotomy Was Used by Author

Through the neck		6
For slipping epiphysis	3	
For coxa vara (fracture in infancy?)	1	
For bony ankylosis	2	
Below the trochanters		9
Open for coxa vara (fracture in infancy)	1	
Open to overcome outward rotation	3	
Subcutaneous (Adams Gant) for tuberculous ankylosis	3	
For bony ankylosis	1	
For flexion deformity (tuberculous, without ankylosis)	1	

cases, aided by low diet, for a period of four or five weeks, (2) in molding by hand, without any anesthetic, the softened bones until their deformity is corrected, and (3) in fixing them in the overcorrected position, feeding the patient a highly nutritious diet, and encouraging active use of the limbs as a stimulus to the deposit of lime salts. It is a method which is particularly applicable to the deformities of rickets in patients less than 3 years of age, and I have employed it in a number of such cases (bow-legs, knock-knees and especially "corkscrew" deformities of the lower extremities) with satisfactory results. In only one patient have I adopted it for bilateral rachitic coxa vara. The improvement in this child, while gratifying and sufficient, was not as marked as may be obtained by osteotomy, in very young children with coxa vara (up to about 3 years of age), Anzoletti's method may be considered a worthy substitute.

*Osteotomy*.—I have adopted osteotomy at the hip in fifteen cases (table 2).

<sup>1</sup> I have to record, as due to operative shock, the only death I have had in an open reduction.

The operation through the neck is best done by open incision to ensure that the section is made at the correct location and in the proper axis. In the three patients with slipping epiphysis (Dilkes aged 13, Saloner aged 14 and Povernick aged 13) I did a cuneiform osteotomy through the neck as near as possible to the site of fracture or to the recently united epiphyseal line. In one patient (Sonak aged 10) with coxa vara probably from fracture of the neck in infancy I also did an open cuneiform osteotomy of the neck. In one patient (Santangelo aged 7½ years) with unilateral coxa vara, from fracture in infancy, I did a subtrochanteric cuneiform osteotomy because the deformity was not in the neck itself but consisted merely in a change of axis between shaft and neck. In two patients with bony ankylosis in bad position (Ford aged 12 with coxa vara from osteomyelitis and Hackett aged 19 with ankylosis in marked external rotation from pyemia) I also did osteotomy through the neck as the disease had been healed so long that there seemed little possibility of relighting of the infection.

I have adopted the operation of osteotomy below the trochanters nine times, four times by open incision and five times subcutaneously.

1 The open operations were one for coxa vara (Santangelo aged 7½ years) previously referred to, and three to overcome outward rotation (Bitto aged 11 from infantile paralysis, Remley aged 13 four years after closed reduction of a congenital dislocation and Wenick aged 13 with bony ankylosis following osteomyelitis). In none of these three patients did I wish to attack the neck directly because in two the joint was normal and in the third I feared to relight the osteomyelitis.

2 The subcutaneous operations include three (Devine aged 14, Dolan aged 13, Shaffer aged 16) for tuberculous ankylosis, one (Walker aged 12) for bony ankylosis from osteomyelitis and one (Quinn aged 17) for flexion deformity without ankylosis, the result of tuberculous arthritis. I believe that subcutaneous osteotomy below the trochanters is a satisfactory operation for healed tuberculous ankylosis in bad position but that it any operation is to be done when there are open sinuses or not very firm ankylosis a reconstruction operation is preferable.

*Reconstruction*—This is the operation that is most widely applicable for relief from disability at the hip joint. Table 3 includes twenty-seven such operations which may be placed in the categories tabulated.

The method of reconstruction I have employed is essentially that of Whitman, consisting in temporary detachment of the great trochanter (with the muscles inserted into it) and its reattachment on the outer surface of the shaft after the stump of the neck has been thrust into the acetabulum previously cleared of its contents (remains of head, scar

tissue, etc.) My first operation of this nature was done in October 1914, but I did not realize the advantages of systematically reattaching the detached trochanter until after the publication of Whitman's paper in 1921. In my early operations, the head and neck were absent, so I merely cleared the trochanter subperiosteally, beveled the upper end of the femur into a point and thrust this pointed end into the acetabulum somewhat after the manner of Krause and of Spiengel. If for any reason the end of the shaft or neck cannot be brought into the old acetabulum, as in some cases of congenital dislocation in adults, a new acetabulum is made at a suitable site and when needed, a roof is formed for the too shallow acetabulum (old or new) by turning down a bone flap from the pelvis over the head, as recently described by Gill. In my first operation by this method of reconstruction in 1914 I secured a very good roof for the head from proliferation of bone where the pelvis was gouged out to deepen the old acetabulum.

TABLE 3—*Reconstruction Operation in Twenty-Seven Cases*

Tuberculosis		12
Fibrous ankylosis	3	
Pathologic dislocation	9	
Pathologic dislocation from old osteomyelitis		6
Dislocation, congenital		4
Slipped epiphysis		1
Nonunion of neck		2
Arthritis, dystrophic		2
		<hr/> 27

The operation of reconstruction is the most efficient method that surgery affords in the treatment for pathologic dislocation, whether tuberculous or septic in origin. The head of the femur usually is deformed if not entirely destroyed in these cases, and without the method described by Whitman, which serves to lengthen the neck, or the method employed by Gill, which deepens the acetabulum, it would be impossible to secure a stable joint. I have not hesitated to employ the operation in the presence of unhealed sinuses in either type of disease, but only in cases in which the infection is dormant. In the case of active infection I should prefer to temporize or to do an excision, if the result of the latter is unsatisfactory, a reconstruction operation may be done later. For fibrous ankylosis in bad position of tuberculous origin, I prefer reconstruction to osteotomy, reserving the latter operation for tuberculous ankylosis which appears to be bony. In cases of dystrophic arthritis (hypertrophic or atrophic) my experience is so far too limited for me to express a decided opinion, but I believe that for otherwise robust and not yet senile adults with hypertrophic arthritis attended by much pain which is uncontrollable by walking apparatus, treatment by reconstruction should offer a satisfactory prognosis. In cases of the atrophic type however which usually are polyarticular, I

doubt that reconstruction of the hip will prove as useful as excision permitting dorsal dislocation of the trochanteric fragment these patients usually are so frail that they cannot well endure the prolonged fixation which a reconstruction operation requires nor will the condition of their other joints allow them much use of the hip For congenital dislocation especially in older children and adults I am using more and more some form of reconstruction operation rather than making persistent attempts to restore the intact but usually deformed head to an acetabulum too small or too low for it I have already discussed this question under the heading of 'open reduction' of congenital dislocation of the hip In one case of coxa vara adolescentium (slipped epiphysis), that of a fat boy aged 14 (Zeller) I adopted reconstruction rather than osteotomy because the head of the femur was so deformed and because the acetabulum was beginning to wander In nonunion of the neck of the femur I have abandoned the use of the bone peg in favor of reconstruction for any patient who will endure the necessary post-operative fixation For the old and feeble as already stated I prefer simple excision of the head

*Transfer of Tensor Fasciae Femoris*—The late Gwilym G Davis my former chief proposed and described the transfer of the tensor fasciae femoris as a remedy for paralytic outward rotation of the femur This operation was later described by Legg The tensor fasciae of course must not be paralyzed itself if the transfer is to be of any value, it is cut from its insertion in the fascia lata, and with its nerve supply intact is attached to the great trochanter Thus it supplants the action of the gluteus medius which is the main internal rotator of the hip In cases of paralytic outward rotation in which the tensor fasciae is not intact a certain improvement may be obtained, as pointed out by Davis merely by attachment of the fascia lata to the great trochanter by means of sutures while the limb is held in internal rotation

#### TECHNIC OF OPERATIONS ON THE HIP

*Exposure of the Hip Lambotte's Incision (fig 1)*—The incision passes from the anterior superior spine to the great trochanter dividing the tensor fasciae femoris obliquely across its fibers the incision is then continued downward and forward through the fascia lata The triangular flap of muscle and fascia is turned forward and the neck of the femur is exposed between the long tendon of the rectus medially and the anterior free borders of the gluteus medius and minimus laterally

This incision gives excellent exposure of the femoral neck and great trochanter and fair exposure of the acetabulum It gives opportunity for dependent drainage at its angle near the great trochanter

This procedure is suitable for (1) acute osteomyelitis invading the hip joint (2) tuberculosis of the joint (3) simple excision of the

head (nonunion, hypertrophic arthritis, etc.) and (4) reconstruction in the presence of a normal acetabulum. In cases of congenital dislocation it is an incision difficult to suture when the limb is in the "frog-position." If it is desirable to make a roof for the acetabulum, Lambotte's incision is inferior to Smith-Petersen's.

*Langenbeck's Incision*—This is a straight incision, centered on the great trochanter, made in the direction of the fibers of the gluteus maximus, while the hip is flexed about to 135 degrees. The muscles are detached subperiosteally from the great trochanter, and the posterior surface of the neck is exposed.



Figure 1

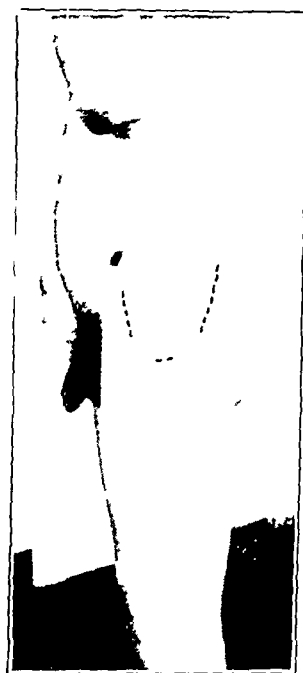


Figure 2

Fig 1—Lambotte's incision for operations on the hip. This photograph was made eight years after excision of the hip for active tuberculosis. See also figures 13 and 14.

Fig 2—Ollier's incision (modified)

Neither this incision nor any other approaching the neck from behind (such as Heyfelder's) is much used in modern surgical procedures. In extremely septic cases of tuberculous arthritis these posterior incisions give sufficient exposure for excision of the upper end of the femur, and they afford direct dependent drainage, but they give inadequate exposure of the acetabulum.

*Modified Ollier's Incision (fig 2)*—The incision is U-shaped, with its rounded curve well below the great trochanter and its two arms extend-

ing upward toward the anterior and posterior superior spines of the ilium, the anterior limb of the incision passes between the sartorius and the tensor fasciae while the posterior limb runs parallel with the fibers of the gluteus maximus near the anterior border of this muscle. The skin and fat are raised in one piece with the underlying fascia lata and tensor fasciae muscle. Then the great trochanter is detached and the gluteus medius and minimus muscles are raised with it and turned upward and forward. The gluteus maximus is not disturbed. This is the incision adopted by Murphy for arthroplasty, and this operation is the main indication for its employment.

*Smith-Petersen's Incision* - (fig 3) —The incision passes along the anterior third or half of the iliac crest to the anterior superior spine, thence downward to a point below the level of the great trochanter between the sartorius and tensor fasciae. The gluteus medius and mini-



Fig 3—Smith-Petersen's incision

mus muscles and the tensor fasciae are cut across below their origins from the ilium, and are then detached subperiosteally from the wing of the ilium, exposing the acetabulum from above. Should better exposure of the great trochanter be desired, the lower end of the incision may be continued backward beneath the trochanter, as in Whitman's incision, to be described.

This incision gives the best possible exposure of the upper border of the acetabulum and of its cavity. It is the best incision for open reduction of congenital dislocation of the hip and for those operations of reconstruction in which it may be desirable to increase the depth of the acetabulum by turning down above it a bone flap from the side of the ilium. The incision in the skin being entirely anterior it is easily repaired even when the limb is in the so-called "frog-position." I have had one case however in which it was impossible to close the soft

2 This is a modern edition with improvements of the incision long known by the name of Sprengel

parts after putting the limb in the frog position, except by bringing the skin from the abdomen down as a curtain over the gap left below the ilium, leaving a considerable hollow space beneath the skin to be filled with blood clot. Healing however was uneventful. It is not a suitable incision for septic cases in which drainage is required, and I should hesitate to employ it in the presence of many old sinuses.<sup>3</sup>

*Whitman's Incision*—Whitman's incision passes from the anterior superior spine downward, then curves backward below the great trochanter, where it ends, having completed half a U. It thus resembles

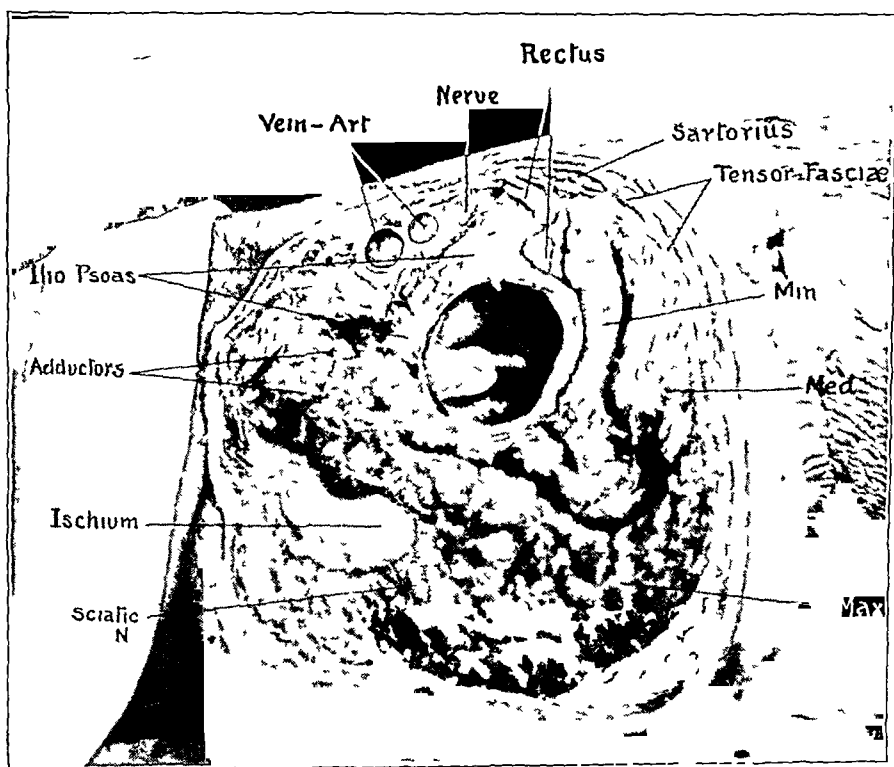


Fig 4—Attachments of muscles around the acetabulum, showing the approach from above, through Smith-Petersen's incision

the anterior part of Olier's incision. Whitman next described the exposure of the capsule through the interval between the tensor fasciæ and the gluteus medius. Surely it is better to incise the fascia lata between the sartorius and the tensor, and to turn back the latter, with intact nerve supply, I have employed this modification in several cases with satisfaction. It provides better exposure of the acetabulum than does the method originally described by Whitman.

3 An incision, merely along the crest of the ilium has served me well, however in cases of extensive necrosis, requiring removal of the ilium down as far as the acetabulum.

This incision (especially if the modification I have suggested is adopted) is admirable for all simple reconstruction operations as it exposes adequately the neck and trochanteric regions. It is desirable it can be converted into Smith-Petersen's incision by continuing the skin incision backward from the anterior superior spine along the crest of the ilium and detaching the tensor fasciae and the gluteal muscles from the pelvis, as previously described,<sup>4</sup> or by continuing its lower end backward and then upward it may be extended into Ollier's incision.

*Opening of the Capsule*—Once the anterior surface of the neck is exposed the surgeon identifies the rim of the acetabulum. I prefer to open the capsule along the upper surface of the neck from acetabulum to great trochanter and then to detach the capsule from the anterior intertrochanteric line. The flap thus made is reflected medially exposing the neck and head of the femur.

*Exposure of the Acetabulum*—1 If the head is still attached to the neck and there is no ankylosis it is delivered by gradual but persistent outward rotation of the femur with the knee flexed and with



Fig 5—Esmarch's gouge fitted with a long handle. Useful in delivering the head of the femur from the acetabulum, and in modeling the head and deepening the acetabulum.

the thigh in increasing degrees of adduction. In the intact hip joint it is difficult to deliver the head until the cotyloid ligament has been freely divided on the head and right up to its pelvic attachment; air then enters the capsule and the force of atmospheric pressure is removed. Usually it is necessary to aid dislocation of the head by cutting the ligamentum teres by means of a gouge (such as Esmarch's, fig 5) or by Lambotte's spoon. To bring the dislocated head well out of the acetabulum, it is necessary to carry the foot of the diseased limb up onto the pelvis or abdomen of the patient with the thigh in marked external rotation and adducted rather than abducted. This brings the empty acetabulum to view.

During these manipulations great care should be taken not to fracture the femur nor (as happened once in my hands) to detach its lower epiphysis.

2 If the head is already absent it is much easier to expose the acetabulum.

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<sup>4</sup> This converts it into an approach to the hip-joint similar to that described by Dupuy de Frenelle.



3 If there is a fracture of the neck and the head remains in the acetabulum, even after the stump of the neck has been delivered into the wound, it is more difficult to extract the head, by the use of Esmarch's gouge, however, it is usually possible to secure its delivery, after cutting of the ligamentum teres. I have found Lambotte's spoon and cork-screw not as useful for this purpose as the large gouge.



Fig 6—Bony ankylosis of the hip from metastatic arthritis (adduction and slight flexion), preservation of normal bone contours makes arthroplasty suitable. See figures 7 and 29 for condition after operation.

4 In cases of ankylosis, the surgeon proceeds as will be detailed in the description of arthroplasty.

*Closure of the Wound*—1 In clean cases it is desirable to repair the capsule by reattaching the inferior border of the reflected flap to the fascia along the anterior intertrochanteric line, and by suturing the posterior margin of the capsule flap to the upper cut border of the capsule.

The various muscles and the fascial layers are then repaired with buried sutures and the skin edges are accurately closed with chromicized catgut without drainage

In most clean cases a plaster of paris dressing is applied before the operation is begun the patient should be put on a table with suitable provision for such a method of fixation



Fig 7—Hip shown in figure 6, five weeks after arthroplasty See figure 29 for range of motion one year after operation The screw remains in place nine years after operation (Arthroplasty, case 8)

In seventy-four operations on the hip joint without sinuses at the time of operation, I have had clean healing in seventy In two cases of tuberculosis a sinus formed after operation, and was slow in healing in one case in which there was a recently healed sinus from osteomyelitis a sinus remained for some months in the operative scar and in the fourth case, a hematoma broke into the incision on the tenth

postoperative day. If the former three cases are omitted because of potential infection before operation, there are seventy-one operations on the hip joint, with only one complication of the wound (discharge of a hematoma).

2 In septic cases the capsule should not be sutured, and the soft parts should be closed only in part, and not too tightly, drainage should

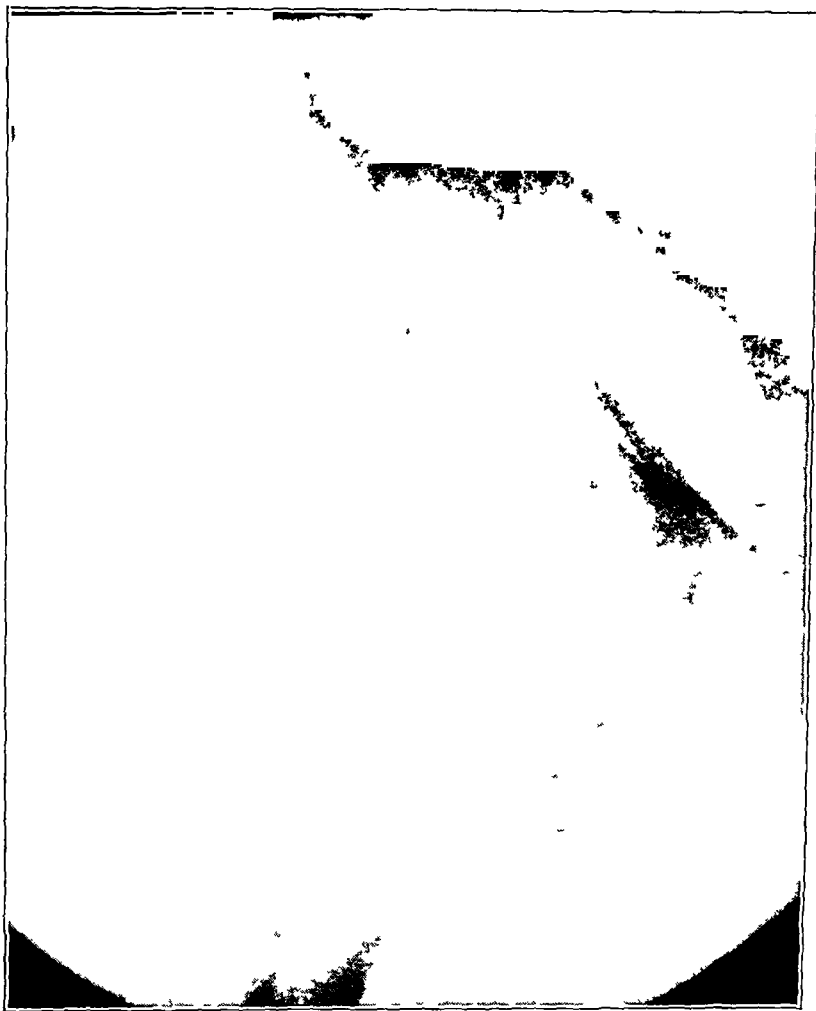


Fig 8—Acute osteomyelitis of the femur invading the left hip-joint. Edward Vedro, aged 12. From roentgenogram made on July 28, 1919, three weeks after drainage of abscess in the adductor region, by another surgeon. See also figures 9, 10, 11 and 12.

be provided at the most dependent portion of the incision, or if necessary by a counterincision. However, I have had uneventful healing in all cases of Lambotte's incision, without the use of a counterincision.

*Arthrodesis*—I have employed several different methods of arthrodesis. 1 In two cases I did Albee's operation (cutting off the upper

surface of the head, and cutting a slice from the upper surface and rim of the acetabulum bringing these two raw surfaces in contact) but succeeded in obtaining ankylosis in only one patient

2 In one case after denuding the head and acetabulum of cartilage I simply fixed the hip in plaster of paris. As ankylosis did not result, I operated on the same patient again nearly four years later this time I transfixed the neck, head and pelvis by two autogenous bone pegs. firm ankylosis resulted

3 In one case I denuded the head and acetabulum of all cartilage and fixed the femur to the pelvis by Lambotte's self-boring screws, bony ankylosis developed.<sup>5</sup>

The difficulty I have found is in keeping the head and acetabulum in contact during application of the fixation dressing, for this purpose in my last case, I employed screw fixation with success

The exposure of the joint is not difficult, especially in cases of infantile paralysis, in which the muscles are atrophied. I have used Lambotte's incision or simply the upper limb of it an anterior incision between sartorius and tensor fasciae or Smith-Petersen's incision. Of these various approaches I prefer Lambotte's

*Arthroplasty*—Little need be added to Murphy's original description of arthroplasty. I have found the modification of Ollier's incision sufficient without adding, in my later operations the "stem of the goblet" recommended by Murphy. The skin and fat are dissected peripherally in all directions so as to expose a still larger area of fascia lata. This structure including the tensor fasciae, is then incised at the limits exposed and is raised along with the overlying flap of skin and fat not being detached from its covering until it is needed toward the end of the operation.<sup>6</sup>

The anterior border of the gluteus minimus and the posterior border of the gluteus medius are next defined, and the great trochanter is detached with a chain or wire saw, or as is often easier with an osteotome and mallet. A large section, preferably all of the great trochanter should be detached, carrying with it the muscles which insert in it however it is not worth while to spend too much time trying to identify the smaller muscles. The anterior surface of the

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5 I may include under the heading arthrodesis, one case of screw-fixation of a recent intracapsular fracture of the femoral neck in a patient with flail-limb from infantile paralysis. bony union was obtained in the fracture and considerable limitation of motion in the hip-joint greatly improving the function (see case 5 under results of arthrodesis)

6 I have used a free flap of fascia lata in two cases only neither operation giving a satisfactory result. Although others have had success with the use of free flaps I should prefer, were I to do the operation again to use the pedunculated flap as described by Murphy

section passes between the attachments of the gluteus minimus and the vastus lateralis. The gluteus maximus is not disturbed. The musculofascial flap, with the trochanter, and still attached to the overlying skin, is then turned upward and forward, exposing the neck of the femur. This exposure is designed to preserve intact the nerve supply of these important muscles, the gluteus minimus, gluteus medius and tensor

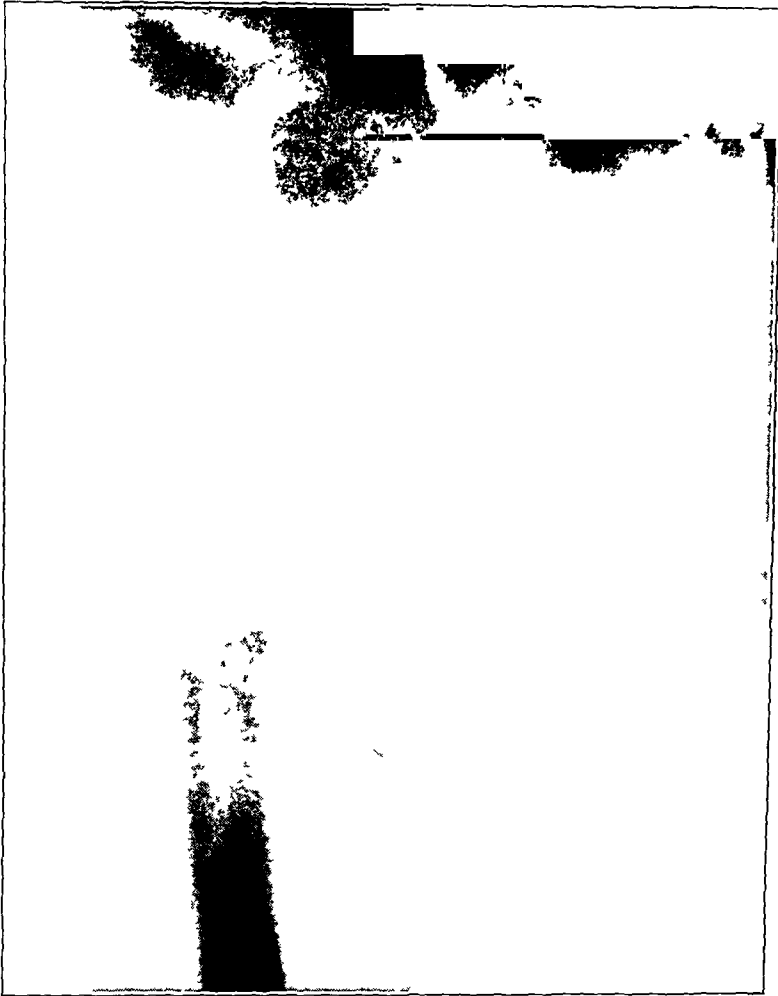


Fig 9—Edward Vedro, aged 12, on Sept 8, 1919, six weeks after excision of the left hip for acute osteomyelitis. Very little bone regeneration. Good position was maintained by weight extension.

fasciae are supplied by the superior gluteal nerve which leaves the pelvis above the piriformis, while the gluteus maximus is supplied by the inferior gluteal nerve emerging below the piriformis.

The remains of the capsule, usually densely adherent, are then detached from the neck, and the junction of the latter with the border of the acetabulum is identified. The bony union is then separated by

means of a large gouge, that known in the shops as Esmarch's is excellent for the purpose especially if a longer handle is provided (fig 5) I have used the same gouge for fifteen years with satisfaction it measures 34 mm from side to side,<sup>7</sup> and its curve is about the same as that of the normal head of the femur its cutting edge is beveled on its convexity thus assuring the excavation of the acetabulum with



Fig 10—Edward Vedro, aged 12, on Oct 14, 1919, eleven weeks after excision of the left hip for osteomyelitis considerable regeneration of bone, taking the form of the trochanters, neck and head

little risk of perforation of the pelvis Care should be taken not to cut the head of the femur too small as it is gradually outlined by the gouge (fig 6) Should it be cut too small it will prove less stable and the acetabulum will therefore have to be enlarged and deepened, this in turn will make the head relatively still smaller If precautions are

<sup>7</sup> Smaller sizes are available for children



Fig 11—Edward Vedro, aged 22, on March 25, 1929 good regeneration of bone ten years after excision of the left hip for acute osteomyelitis See also figures 8, 9, 10 and 12

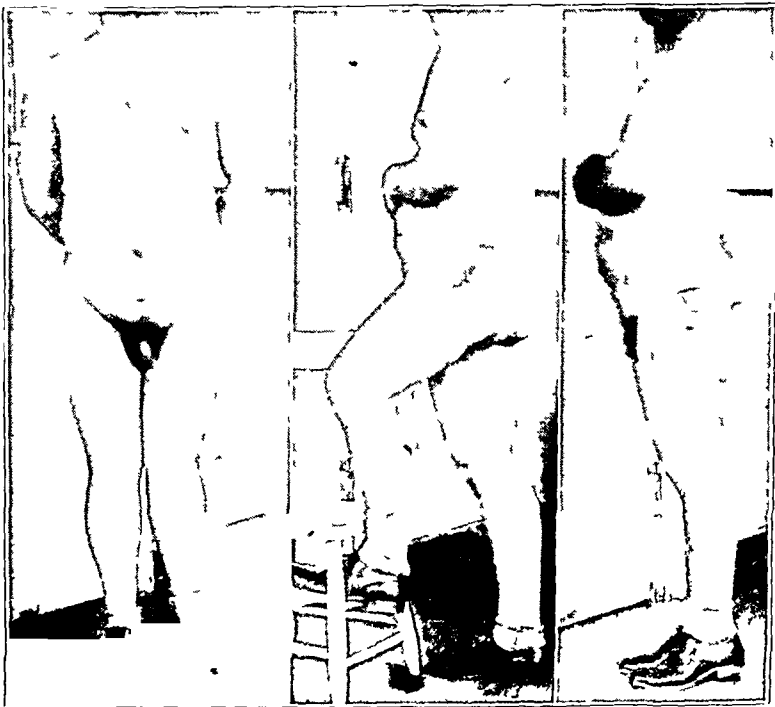


Fig 12—Edward Vedro, aged 23, ten years after excision of the left hip for acute osteomyelitis good station, slight limp, flexion to 135 degrees, full extension, rotation very limited, no disability (Same patient as in figures 8, 9, 10 and 11)

taken to cut the head amply large in the first place the surgeon can afford to sacrifice some of its surface in remodeling it if it is not of proper shape when formed. There is little danger of cutting too deeply into the pelvis with this gouge as the pelvis is much thicker in this region than is usually realized. Even should the base of the acetabulum be perforated as occurred to me in one case (of reconstruction of the hip) no harm need result. After almost all the bony ankylosis has been divided by the gouge it usually will become possible to break the remaining fibers by gentle manipulation of the femur taking care of course not to fracture the bone elsewhere than at the joint level. The head finally freed from the pelvis, is luxated anteriorly as already

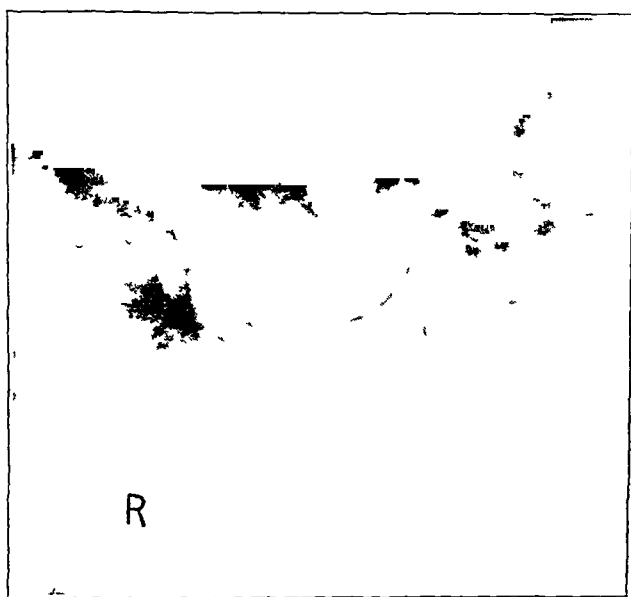


Fig. 13—James Fleet, aged 37 on Feb. 2, 1927, eight years after excision of the left hip for acute tuberculosis with sinus. See figure 14.

described and is modeled to proper shape and the acetabulum is reamed out so as to accommodate it securely and without any tension, leaving room for the interposition of the flap of fascia lata. I have not had as much satisfaction from the use of Murphy's end-mill and reamer as from modeling by means of Esmarch's gouge. When by repeated trial it has been found that the head of the femur fits easily and securely into the acetabulum the fascia lata is dissected away from the overlying skin and its pedicle is somewhat narrowed at the expense of its anterior attachments (tensor fasciae). This is necessary in order to allow it to be brought into the acetabulum without tension around the posterior border of the gluteus medius since this muscle



and the great trochanter are to be reattached to the femur. The flap of fascia lata thus prepared is spread over the acetabulum and is attached with sutures to any available tissues around the rim of the acetabulum. The head of the femur is then replaced on this fascial bed, and the great trochanter, with its muscles, is brought down and is reattached at its original site with one or two of Lambotte's self-boring screws (fig 7). If two screws are inserted at different angles one serves to bind the other (fig 24 B). Finally, the skin and fat are closed. No drainage is employed.

I have found that the actual operation takes just over one hour. Weight traction (Buck's extension) is applied at once, and the weight



Fig 14—James Fleet, aged 39, on Feb 24, 1929, ten years after excision of the left hip for tuberculosis. Flexion to right angle, full extension, shortening 15 cm, moderate limp, no disability. Out of work for about eighteen months after operation.

is increased rapidly up to a total of about 8 or 10 Kg. The hip is not otherwise immobilized. After from four to six weeks, active motion is encouraged, and gentle passive motion (just short of pain) may be made by the surgeon himself. At the end of two months, walking with crutches may be allowed, the weight extension being resumed every night. Only after walking has been learned do I believe it is proper to resort to vigorous mobilization. My experience has been that patients either do well and get fairly free motion without trouble, or they do badly and the hip remains stiff and painful. In the former cases active physiotherapy is not necessary, and in the latter it is useless.

*Bone Pegs*—I have employed bone pegs at the hip five times for nonunion as well as once in an effort to produce arthrodesis, as previously mentioned. I prefer to cut the pegs from the subcutaneous surface of the tibia rather than from its crest or from the fibula. I have seen one or two fractures occur in the tibia after bone had been cut from its crest and hence prefer to leave this strong buttress intact. I have used pegs from the fibula only twice and in one case found the bone from the fibula so atrophic that it was difficult to drive it into

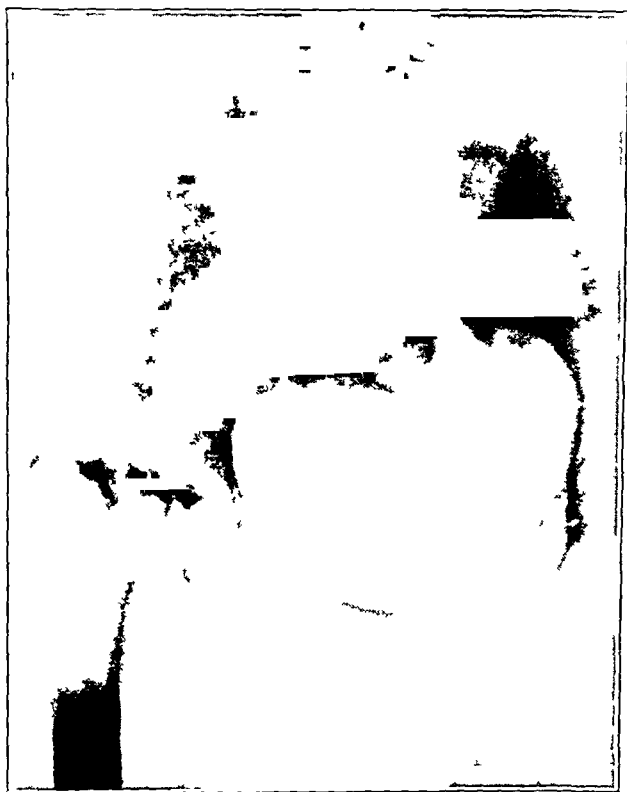


Fig 15—Antoinette Stellone, aged 17 on March 18, 1929 three years after reconstruction of the right hip for congenital dislocation. The head was removed the stump of the neck implanted in the false acetabulum and the trochanter transplanted lower on the shaft. The hip is stable, fair motion, shortening 15 cm, moderate limp, no pain.

the hole prepared for it. It is better to put a square or triangular peg into a round hole because it becomes firmly fixed at once whereas either the head or the neck of the femur may rotate about a round peg. Nor do I regard it as desirable to include the periosteum with the transplant. I am convinced that periosteum acts merely as a limiting membrane and therefore prevents penetration of the transplant by the

cells of the bone into which it is implanted. Only when a transplant is to be used to bridge a gap—in other words, when it forms what I have called a supplant—am I in the habit of leaving its periosteum in place, under these circumstances, it seems to me that the periosteum can serve a useful rôle by protecting the bone supplant from destruction (at least on one surface) by the foreign tissues, not osseous, among which it is placed.

*Bone Implants*—In the patient with fibrous osteitis of the neck and trochanters, to whom I have previously made reference, I made an incision over the great trochanter, opened the cortex, cleared out the old scar tissue from the interior of the bone up to the head and implanted into the cavity two bone transplants, one of which was driven downward into the shaft and the other upward into the head.

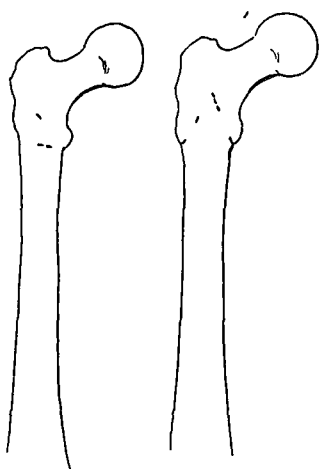


Figure 16      Figure 17

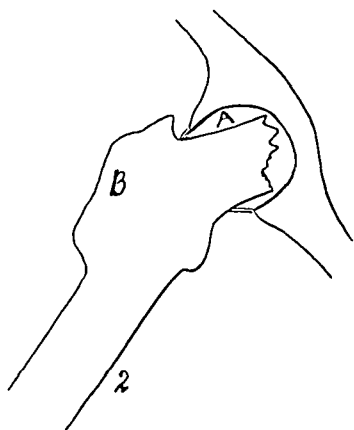
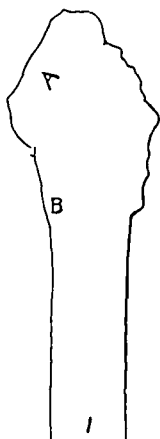


Figure 18

Fig 16—Diagram of subtrochanteric (cuneiform) osteotomy of the femur, to overcome adduction

Fig 17—Diagram of subtrochanteric osteotomy by inverted *V* incision, to overcome external rotation

Fig 18—Diagram of Whitman's operation of reconstruction of the hip (1) The trochanter is detached, thus providing a lengthened neck (2) The lengthened neck is placed within the acetabulum, and the trochanter is reattached to the femur below its original site

*Capsulorrhaphy*—For capsulorrhaphy (which I described in 1921) an incision from the anterior superior spine of the ilium to the great trochanter is used, the tensor fasciae being divided or retracted and the capsule anterior to the border of the gluteus medius being exposed. Then the long tendon of the rectus femoris is retracted medially and the dislocated head is reduced. Next an incision is made through the capsule from the anterior inferior spine parallel with the neck of the femur as far as the lateral end of the anterior intertrochanteric line of

the femur. If the patient has been up and about until shortly before the operation there may be considerable excess of joint fluid from trauma due to recurrent dislocation. After the joint fluid has been wiped away the capsule is detached from its insertion along the anterior intertrochanteric line, and the triangular flap of capsule thus formed is drawn laterally and posteriorly superficial to the unopened portion of the capsule on the upper surface of the neck, this portion of the

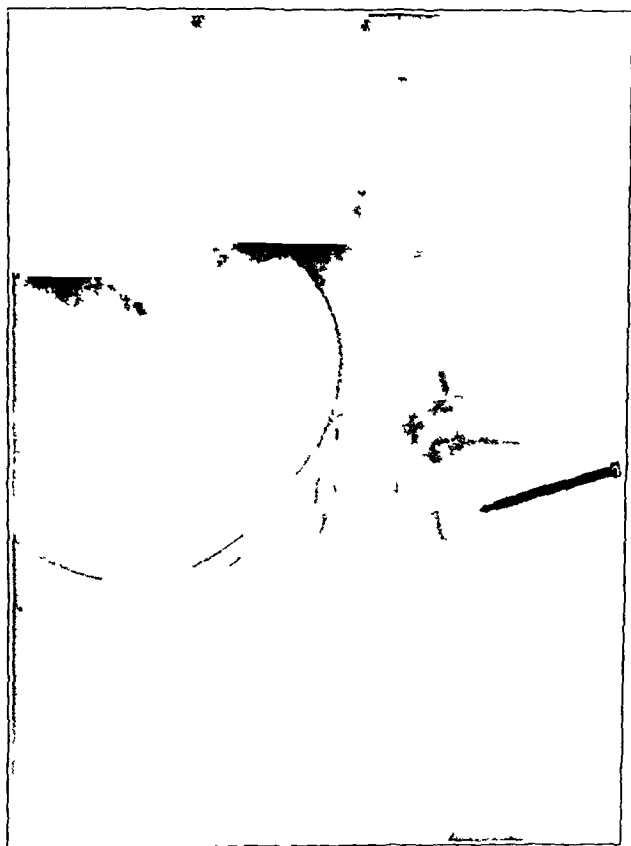


Fig 19—Henrietta Eichelberger aged 36, on April 7, 1929, five years after reconstruction of the left hip for nonunion of the neck of five months duration was out of heavy work for one year after operation shortening 1 cm slight limp, toes forward flexion to 110 degrees full extension rotation normal Climbs easily over fences and on to chairs Some stiffness in damp weather

capsule has become thinned and stretched by the upward pressure of the dislocated head in the patient's attempts at walking. The flap of the capsule is thus overlapped over the weakened portion and is held securely in place with mattress sutures of chromic catgut. In all three of my patients I have found that when this suturing was completed it was impossible to luxate the head even when efforts were made to do

so with the femur in adduction, previously the most unstable position. After closure of the soft parts in layers, the hip is dressed in plaster of paris while in abduction. The limb is protected by plaster for about three months, and walking is gradually resumed. All my patients have had rather extensive paralysis lower in the same limb, and in two of them both lower limbs were the site of infantile paralysis.

*Excision*—I have used many different incisions for excising the head of the femur, but I prefer that of Lambotte, this gives adequate exposure and ample provision for drainage, in septic cases, from the angle of the incision.

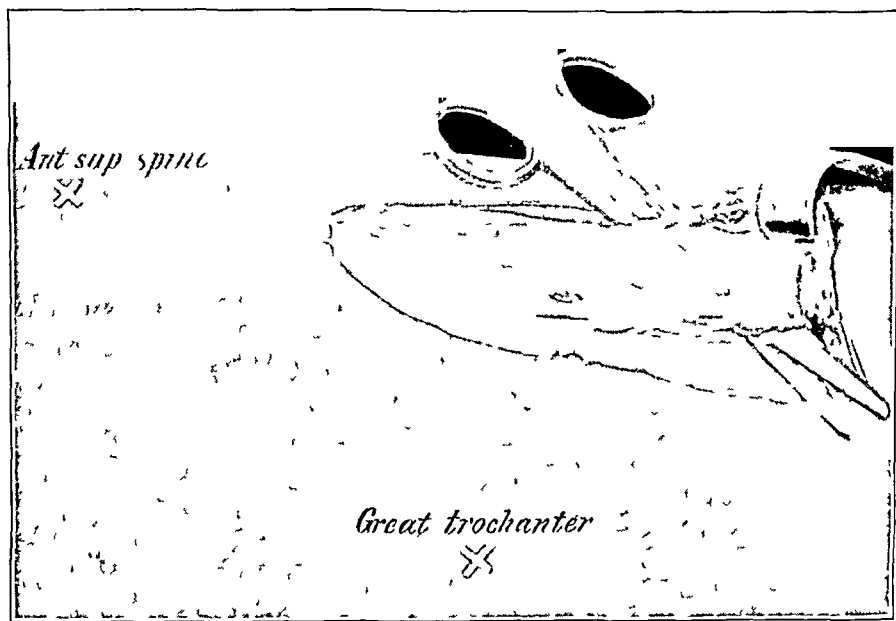


Fig. 20—Transfer of tensor fasciae latae to great trochanter, to overcome paralytic outward rotation right hip. The scissors pass under the tendon of the tensor fasciae.

For Septic Osteomyelitis or Tuberculosis. The capsule is already ruptured, the head often lying loose in the acetabulum as a sequestrum. The head is easily removed by the fingers, a curet or sequestrum forceps. Then so much of the neck and trochanteric portions of the femur are removed as seems indicated to secure free drainage of the hip joint. The bone should be removed subperiosteally so far as possible, in the hope that some of it may regenerate. This regeneration is the rule, at least to some extent, in cases of septic osteomyelitis (figs 8, 9, 10, 11 and 12), but it may also occur in some cases of tuberculosis. The joint is drained by a tube the upper limb of the incision being closed by interrupted sutures, but most if not the whole of the lower limb is left unsutured. Buck's extension is applied, and

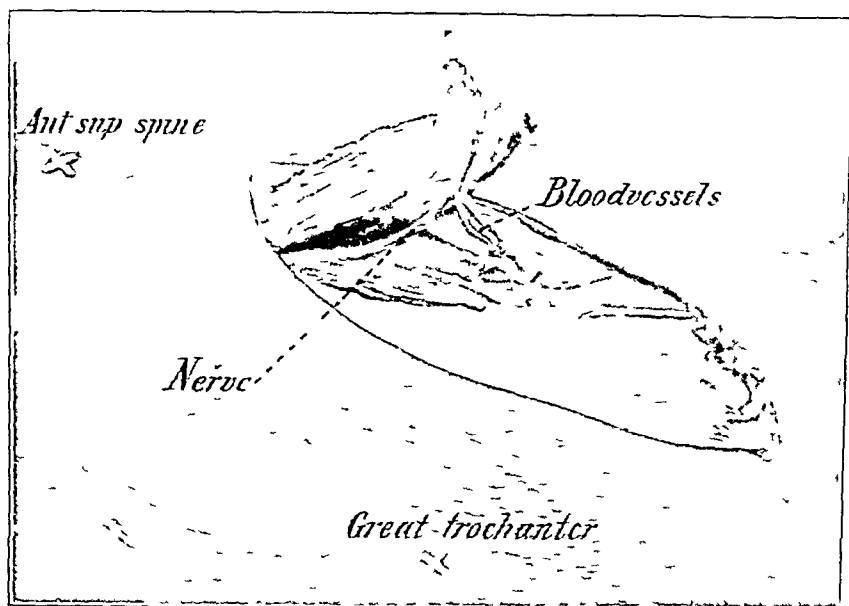


Fig 21—Transfer of tensor fasciae The tendon has been cut and the muscle raised, carefully preserving its innervation

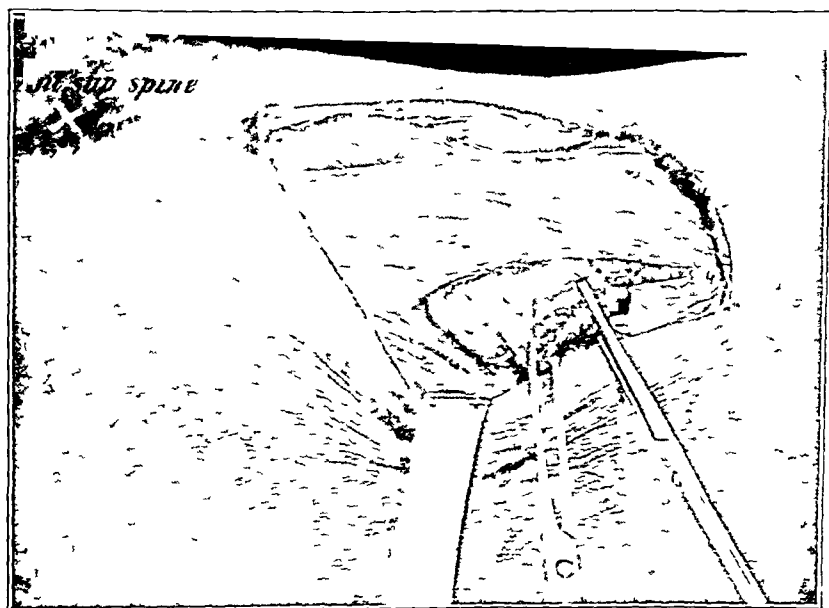


Fig 22—Transfer of tensor fasciae The muscle is drawn beneath the iliotibial band and through an incision in the fascia lata posterior to the iliotibial band The muscle is then sutured to the great trochanter and to the overlying fascia while the limb is held in slight internal rotation

the limb is immobilized in moderate abduction and nearly full extension. Recumbency is continued until the hip becomes stable, and the drainage tract is nearly or quite healed. This may require several months. The patient is then allowed to be about with proper apparatus, which may be discarded in most cases in a year or eighteen months. The patient may require a crutch or a cane for some time longer, but usually within a year or two he is able to be around without support (figs 13 and 14).

For Nonunion of Fractures of the Neck. The Lambotte incision is used, but as the capsule is not already perforated, it must be opened. This is best done parallel with the neck and thence medially and laterally along the anterior intertrochanteric line. Next the line of

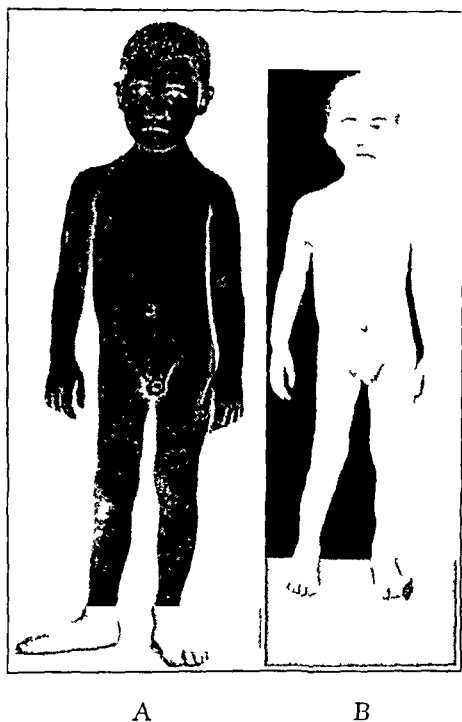
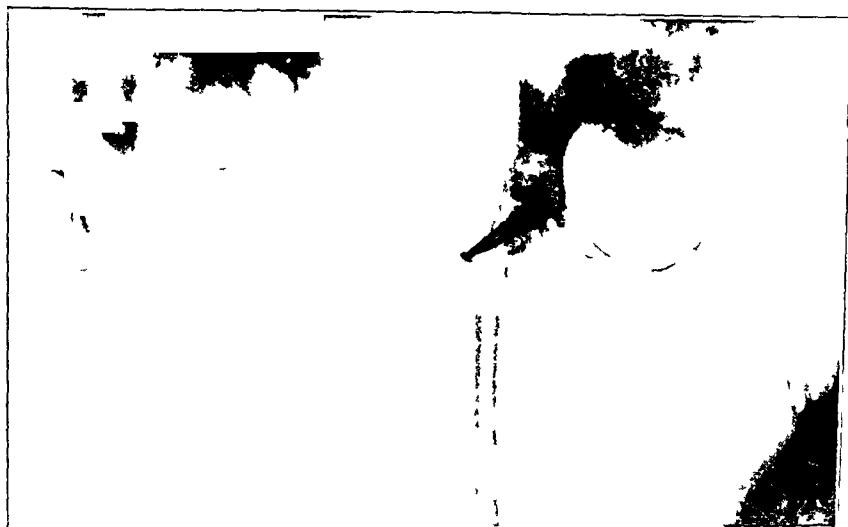


Fig 23—*A*, paralytic outward rotation in a boy (Arthur Simpson), aged 6 years. *B*, same patient two months after transfer of tensor fasciae into great trochanter. The result was maintained fourteen years later.

fracture is identified and is opened with a periosteal elevator or chisel, by strong outward rotation of the thigh, it is possible to expose the fractured surface of the head. The capital fragment may slip back and forth in the acetabulum, and unless proper instruments are provided may be difficult to extract. In using Lambotte's corkscrew (devised by him for this purpose) I have been a little disappointed to find that it will not catch hold in a very atrophic head, nor have I found that Lambotte's spoon used in conjunction with the corkscrew, much facilitates the extraction of the head. On the whole, I have found it



A

B

Fig 24—*A* Joseph Thomas aged 13 flail-hip from infantile paralysis *B* same patient one year after arthrodesis and fixation by two Lambotte self-boring screws The screws are still in place two years after operation

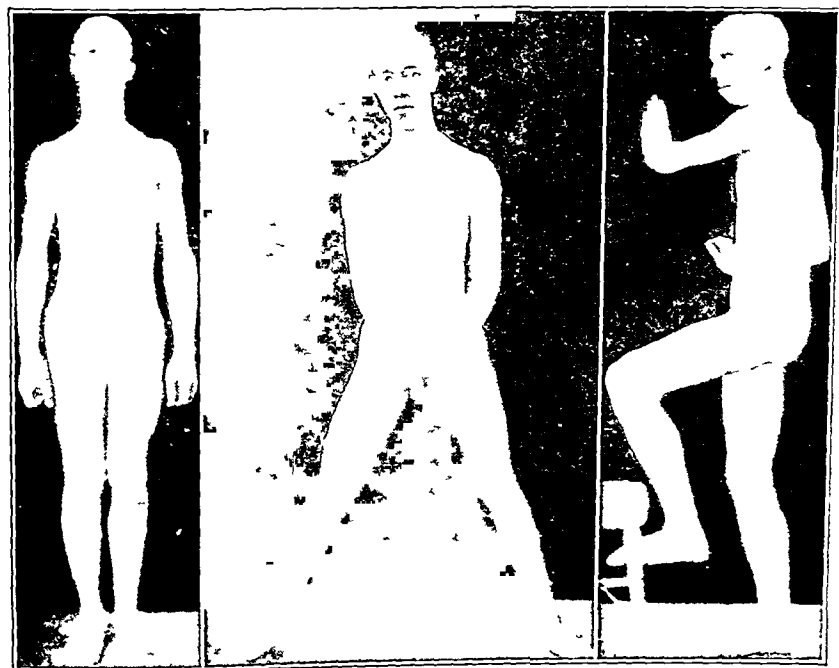


Fig 25—Arthroplasty case 1 Joseph Hall aged 20 (1916) one year after arthroplasty of the left hip for bony ankylosis from gonococcic arthritis



easiest to depend on Esmarch's large gouge, with which the ligamentum teres may be cut and the head levered out of the acetabulum with little difficulty

When the head has been extracted, the capsule is closed, and the incision in the soft parts is sutured in layers, without drainage. Buck's traction apparatus is applied, and the limb is kept in moderate abduction and full extension. The patients may leave bed as soon as the soft parts are firmly healed, by the end of the third week, they should be able to be about with crutches.

*Open Reduction*—For a long time I used Lambotte's incision in doing open reduction of congenital dislocations of the hip, but I found



Fig 26—Arthroplasty, case 6, Marie Davenport, aged 16 (1915) bony ankylosis from "typhoid fever" six years previously (staphylococcic osteomyelitis). See figure 27

it so inconvenient to suture this incision while the limb is held in flexion and abduction (the so-called "frog position") that I have been glad in my later operations to use Smith-Peterson's incision (1917) which is a modification of, and an improvement on, that described by Sprengel in 1897 (figs 3 and 4)

1 In the cases of recurrent luxation, subluxation or simple incongruence between the head and the acetabulum, it is often sufficient, as Gill pointed out merely to turn down over the too shallow acetabulum a roof of bone with its attachment close to the upper lip of the acetabulum. The surgeon enters his chisel or gouge as far above the acetabulum

as he wishes the width of this roof to be cutting rather deeply into the pelvis (the bone just above the acetabulum is thick) he outlines cautiously a flap of bone and gradually pries its upper border loose from the pelvis taking great care not to fracture its lower attachments entirely free. To hold this roof down over the head Gill takes tree transplants (chips of bone) from the already bared iliac crest and wedges them into the gap between the bone flap and the pelvis. The hip is dressed in plaster of paris in the flexed and abducted position and the soft parts are closed in layers without drainage. The after-treatment is conducted as usual in cases of congenital dislocation of the



Fig 27—Same patient as in figure 26, five months after arthroplasty

hip in childhood. Both hips should not be operated on at the same sitting. An interval of several months should be allowed to intervene.

2 In cases of irreducible congenital dislocation in children less than 10 years of age, it is necessary to open the capsule incise the hourglass constriction between the pouch in which the head lies and the acetabulum, and usually to clear the latter of cartilage and debris. If the head cannot be made to enter the acetabulum without undue force or repeated attempts at reduction the surgeon will do well not to persist in such attempts but to resort to one of two remedies: (a) to remove the head, transplant the trochanter and thrust the end of the neck into the acetabulum (i. e. the reconstruction operation) or (b) to make a new acetabulum above the old into which the head or

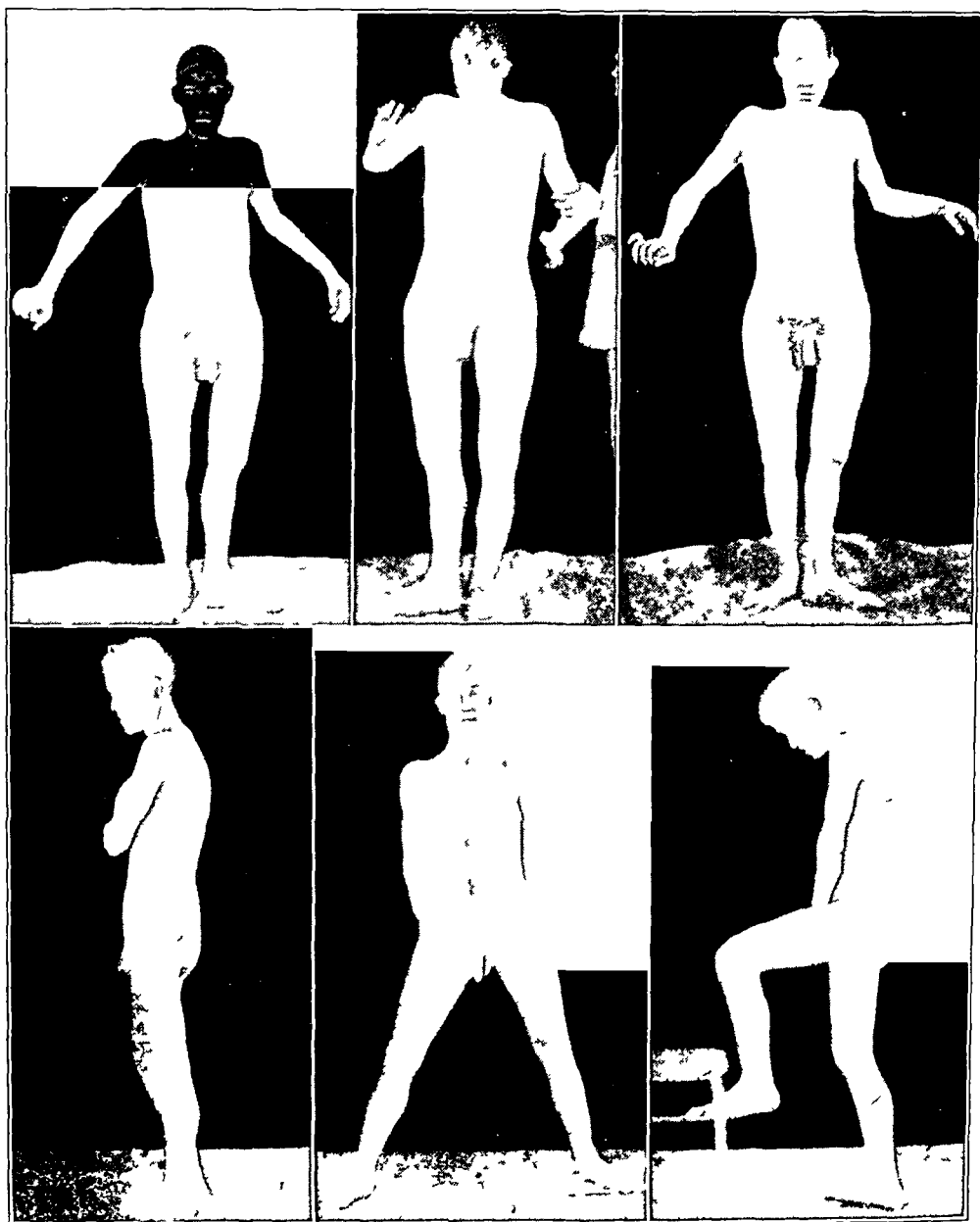


Fig 28 — Arthroplasty, case 7, Charles Lamb, aged 22, pathologic dislocation of the left hip following acute polyarthritis one year previously. Upper photographs (1917) before arthroplasty, lower photographs two and one half months after arthroplasty.

the stump of the neck can be placed without difficulty (fig 15). As already stated in one of my cases death occurred from shock due to prolonged efforts at reduction in a girl aged 13.

*Osteoclasis* (Anzoletti).—The technique of osteoclasis has already been described.

*Osteotomy*.—*Open Osteotomy Through the Neck*. I have usually employed an incision from the anterior superior spine to the great trochanter. In fat patients this scarcely gives sufficient exposure but the incision may be extended easily into Lambotte's typical incision, or one may use the incision of Smith-Petersen. The capsule is exposed lateral to the long tendon of the rectus; it is opened in the long



Fig. 29.—Arthroplasty, case 8, Mary Bailey, aged 22, eight months after arthroplasty for bony ankylosis from gonococcic arthritis. (See figures 6 and 7 for roentgenograms of this patient.) Traced for nine years, no limp, no disability, flexion to 90 degrees, full extension, abduction 20 degrees, rotation free.

axis of the neck along the upper border of the latter and is detached from the anterior intertrochanteric line, the flap of capsule is turned forward. The neck thus exposed usually is found (in cases of coxa vara due to epiphyseal separation of the head or in those due to fracture of the neck in infancy) to present an anterior and a superior convexity, the limb being in outward rotation. In one case (Dilkes) I saw a distinct line of fracture at the apex of the cervical deformity, even though the injury dated back two years. In the cases due to epiphyseal separation of the head there is little or no motion in the joint. In cases of fracture through the neck in infancy there is usually free flexion and

extension, only abduction being lost<sup>8</sup> The wedge of bone to be removed from the deformed neck should be carefully calculated as to its width, its depth and its direction so that the gap may be accurately closed by abduction and internal rotation of the femur In cases of epiphyseal separation the capsule is adherent to the neck, but in fractures of the neck it is not, and after the osteotomy it may be closed by



Fig. 30—Bone peg for nonunion, case 3, Isaac Bachr, aged 52, nonunion for twelve months

8 My observations confirm those of Whitman, who pointed out that in cases of fracture of the neck usually occurring before the age of 10 years, there had been a severe injury followed by immediate disability, but that later there remained only lost abduction fixed external rotation, limp and shortening, flexion and extension being preserved, whereas in cases of epiphyseal separation of the head, which occurs after 10 years of age there is a history only of slight injury, with little immediate disability but that the hip becomes stiff in external rotation, due to disorganization of the joint

suture. The limb is dressed in abduction in plaster of paris and is immobilized for two months at least. Even in cases of epiphyseal separation a fair range of motion may be expected to develop but not such free motion as in cases of fracture of the neck. Of course if bony ankylosis (from osteomyelitis or other cause) exists at the time of the

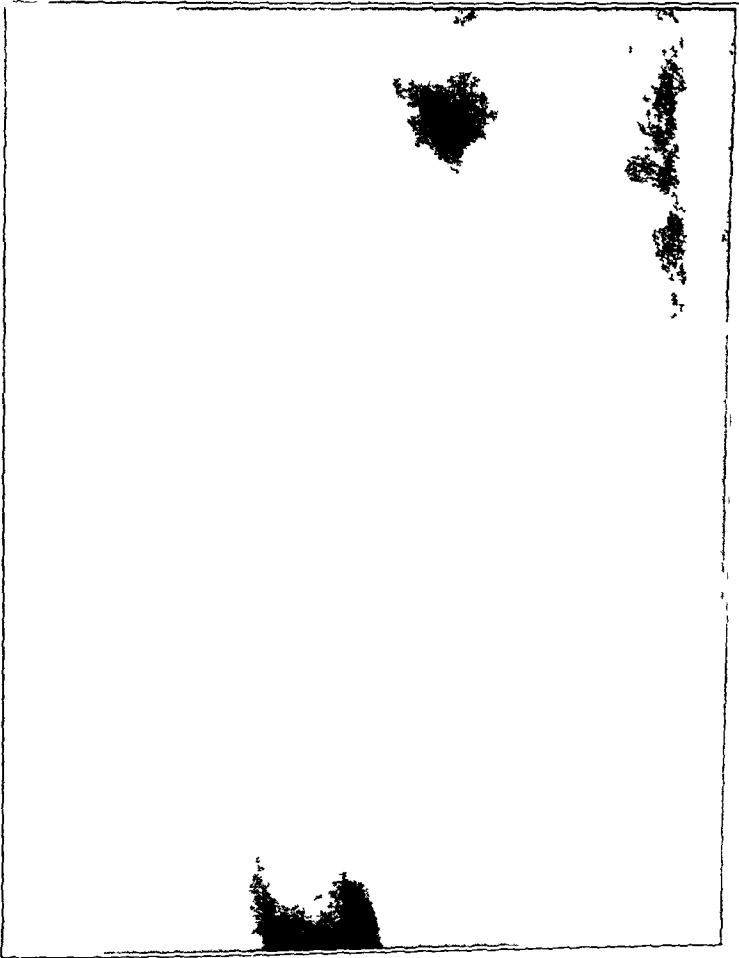


Fig. 31—Same as figure 30, two and one-half months after operation

operation, all that osteotomy accomplishes is improvement of the position of the limb, as regards both external rotation and adduction.

**Open Osteotomy Below the Trochanters.** Sufficient exposure is obtained by a straight incision of moderate length along the outer surface of the great trochanter. If the femur is in marked external rotation, this incision will expose the anterior rather than the lateral surface of the shaft, and the proper intermuscular space should be sought.

(a) If correction of adduction alone is desired, a wedge is removed from the lateral border of the femur between the two trochanters, care being taken not to deepen the wedge too far toward the median border and to make all the bevel of the wedge at the expense of the upper fragment, cutting the distal section transverse to the long axis of the shaft (fig 16). Enough bone fibers should be left intact on the median border to allow a greenstick fracture to be produced, thus preventing the lower fragment from slipping past the upper into the adductor region. This accident occurred in one of my patients, but owing to his youth ( $7\frac{1}{2}$  years) no disability resulted except some increase in the shorten-



Fig 32—Same patient as in figures 30 and 31, one year after operation

ing of an already short extremity, in accordance with Wolfe's law, the displaced fragments became well rounded off, union was bony and all the movements in the joint had nearly their normal range

(b) If correction of external rotation only is desired, I have found it useful to divide the femur by an inverted V osteotomy, owing to the spongy character of the bone the lower fragment may then be rotated inward on the upper, without fear of separation of the ends of the bone (fig 17)

Subcutaneous Osteotomy of the Femur for Deformity at the Hip  
I have never employed subcutaneous osteotomy through the neck of the femur the original Adams' operation (1871), as I prefer the sub-

trochanteric site recommended by Gant (1872) though I use Adams' knife and saw in preference to the osteotome used by Gant. In tuberculous ankylosis in which cases particularly this method is advisable to correct deformity, I believe that there is less risk of causing a renewal of trouble in the hip joint after the operation with the saw than when a hammer and osteotome are employed. The only instruments required are the knife and the saw originally used by Adams, the knife with a short blade and a long handle is inserted directly against the outer



Fig. 33—Excision of the right hip for acute osteomyelitis case 4. Fred Freund, aged 17, roentgenogram three and one half years after operation. Upper end of femur not in acetabulum.

surface of the femur just below the level of the lesser trochanter (about 4 cm. below the tip of the great trochanter). This is nearer the pelvis than in the normal case owing to the destruction of the head and neck of the femur by disease. The knife is then carried across the anterior surface of the femur clinging closely to the bone and not passing beyond its medial surface into the adductor region. Before this knife is withdrawn Adams' saw (one with a very short cutting surface) is





Fig 34—Same patient as figure 33 hip stable and in good position, good range of motion

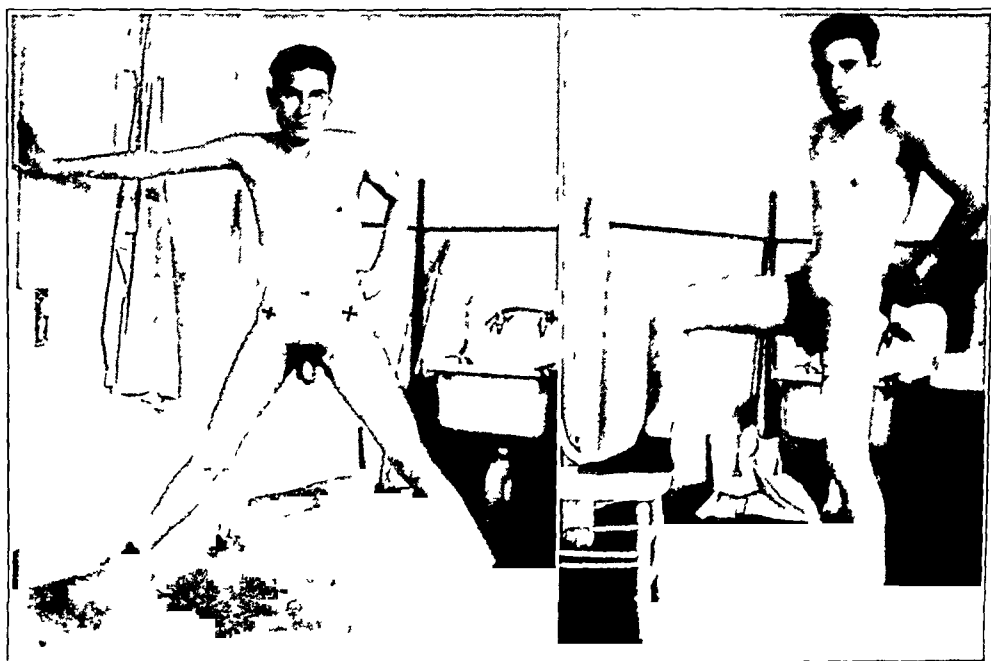


Fig 35—Jacob Saloner aged 17, in September, 1928, three years after cuneiform osteotomy of the neck of the right femur for coxa vara from slipped epiphysis See figure 36

introduced alongside the knife through the same puncture in the skin and when the saw can be felt in contact with the anterior surface of the femur the knife is withdrawn. Then the surgeon saws about two thirds of the distance across the femur from its anterior toward its posterior surface making very short excursions with the saw as required by the shortness of its blade. The saw should be used gently. The operation may be tedious but it is safe. In the course of the actual time of sawing has consumed from five to ten minutes. When the surgeon thinks that the femur is sawed through he should try gently to fracture the remaining piece of bone with the saw. If the saw is once removed it will probably be difficult to

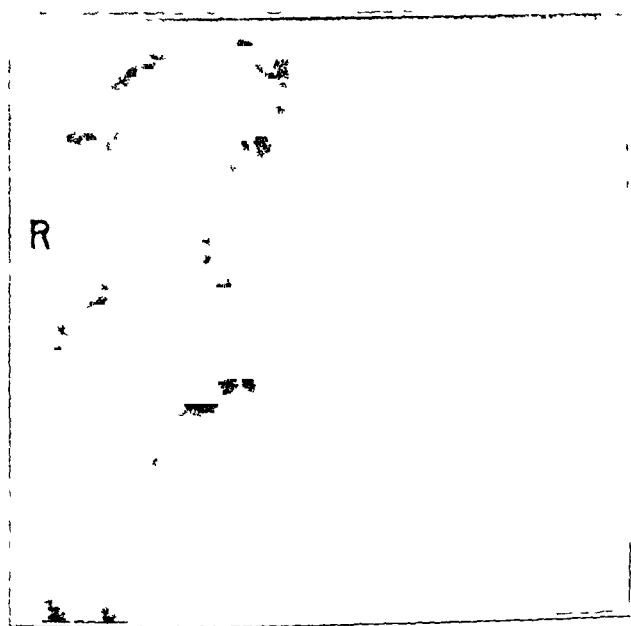
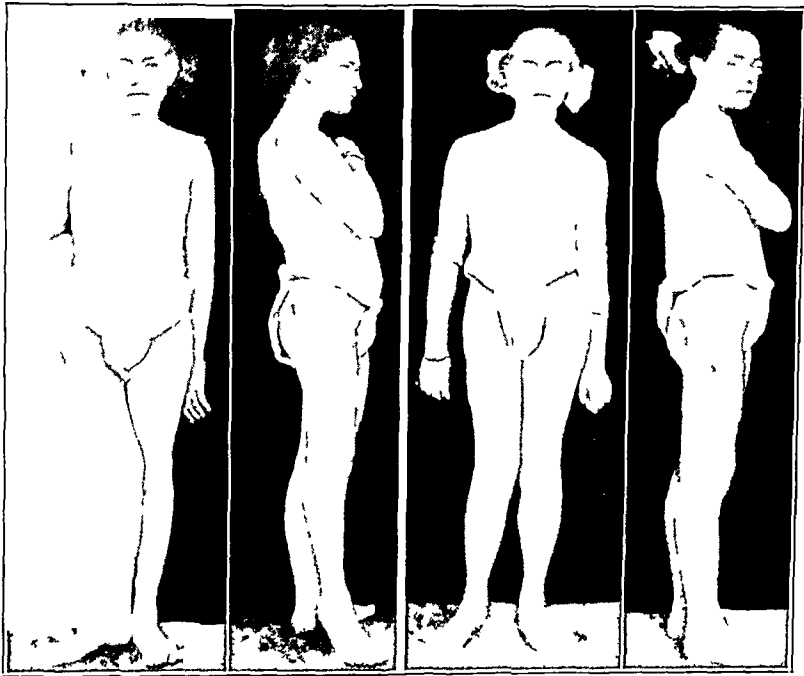


Fig. 35—Same patient as in figure 35

or impossible to insinuate it again into the saw line previously cut. I have never had the opportunity to try my skill at reinserting the saw because I have found the femur easily broken in all cases before removal of the saw. It is helpful to have the sound limb flexed firmly on the pelvis in order to steady the latter, while the greenstick fracture of the femur on the deformed side is completed. The wound which is a mere puncture, requires only a single suture. If desired the limb may be brought further into abduction by the subcutaneous tenotomy of the adductor muscles, close to their origin from the pelvis.

*Reconstruction*—I have used Lambotte's incision in twenty-one of twenty-seven operations for reconstruction, in four I have used Smith-Petersen's incision and in two the modification of Whitman's incision

which I have already described. I have preferred Lambotte's incision especially in pathologic dislocations due to tuberculosis and those following septic osteomyelitis, with open sinuses. I believe that this incision is less apt to spread infection into the soft parts than Smith-Petersen's incision. The latter, however, has the great advantage of exposing the pelvis above the acetabulum, the region whence a roof of bone may have to be turned down, hence it is preferable to Lambotte's or to Whitman's (modified) incision in many cases of congenital dislocation. Whitman's modified incision gives adequate exposure for a simple reconstruction operation alone, and anatomically is more correct



A

B

Fig 37—Osteotomy below trochanters for ankylosis in outward rotation, from osteomyelitis. Rose Wenick, aged 14 years. *A*, before, *B*, after operation.

than Lambotte's in that it turns the entire tensor fasciae muscle backward instead of dividing it. I should have used it oftener had I not been familiar with Lambotte's method before Whitman published a description of his reconstruction operation.

Exposure having been gained, the head of the femur (if not previously destroyed by disease or removed by operation) is excised and the great trochanter is cut off with an osteotome or saw at such an angle as may serve to provide the longest stump of neck for insertion into the acetabulum. The section of the trochanter usually should be made parallel with the upper border of the neck (fig 18), hence



Fig 38—*A*, osteotomy below the trochanters of the right femur to overcome outward rotation, four years after bloodless reduction of congenital dislocation of both hips. The patient was 13 years old at the time of operation in 1925. The roentgenogram was taken in 1929, when the patient was 16. *B* before and *C*, three years after osteotomy of the right femur to overcome outward rotation. The left femur is still in outward rotation.

the neck should be well cleared before the trochanter is detached. The acetabulum is next cleared of scar tissue, and is deepened if necessary by gouge. Then the stump of the neck is placed inside the acetabulum, Esmarch's gouge being used as a combined lever and skid if reduction cannot easily be made by manipulation alone. In cases of pathologic or congenital dislocation, the previous detachment of the trochanter makes it much easier to bring the stump of the neck down to the normal acetabulum. The thigh is now kept in moderate abduction (from 20 to 30 degrees) while an area on the lateral surface of the shaft of the femur is denuded of its periosteum, and the great trochanter is

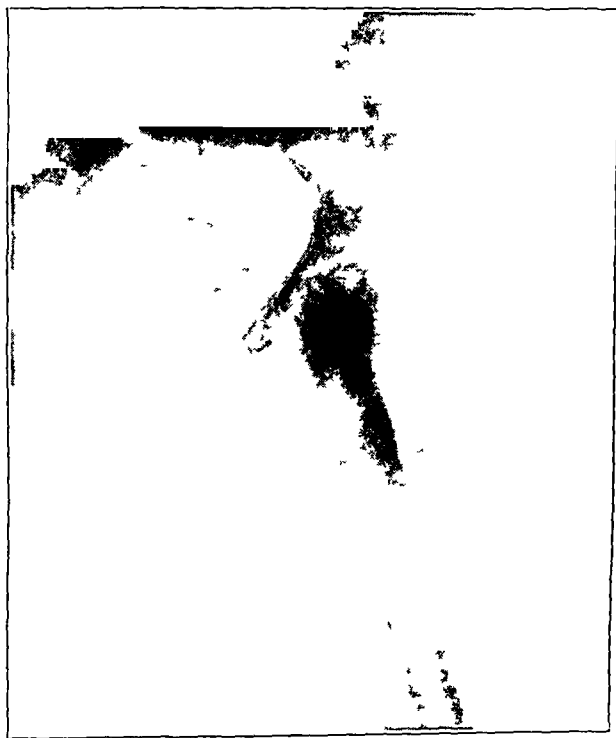


Fig. 39—Recent subcutaneous subtrochanteric osteotomy (Adams-Gant) for ankylosis in flexion following a reconstruction operation for pathologic dislocation (reconstruction for tuberculosis, case 7), seven years previously. Betty Shaeffer, aged 16.

applied against it. In many cases it is sufficient to suture the fascia and muscles over the trochanter, which stays easily in its new position, but if it does not fall easily into place it may be sutured to the femur by chromic gut, or may be fixed to it by means of Lambotte's self-boring screws (fig. 19). Of course, the latter should not be used in tuberculous or septic cases. The soft parts are then closed in layers, without drainage, and the limb is fixed in plaster of paris in the stable position of abduction.

If it is evident that the femur cannot safely or successfully be restored to the acetabulum the surgeon will have to utilize the false acetabulum in which it already articulates (fig 15) if none such exists he will have to make a new one preferably near the anterior inferior spine so as to bring the axis of weight-bearing sufficiently far forward on the pelvis to prevent continuance of the back strain from the lordosis which was present before the operation was undertaken. In either case, if the new acetabulum cannot be made sufficiently deep or

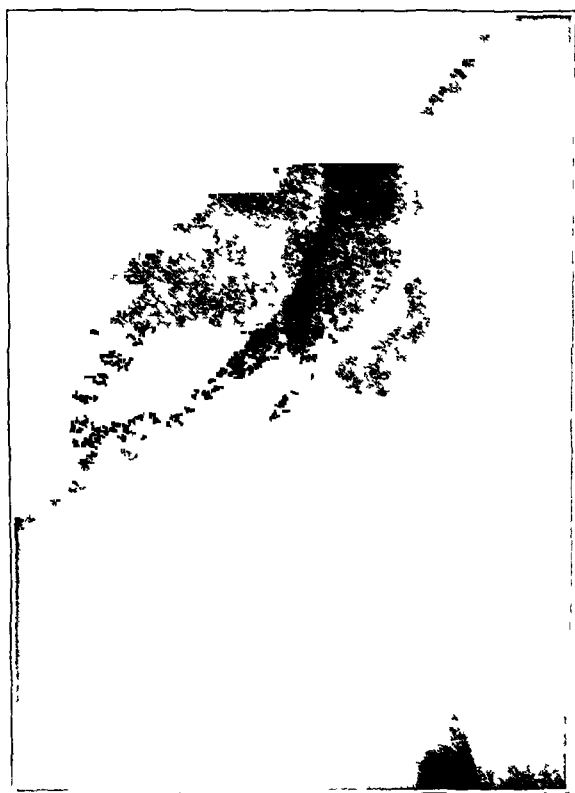
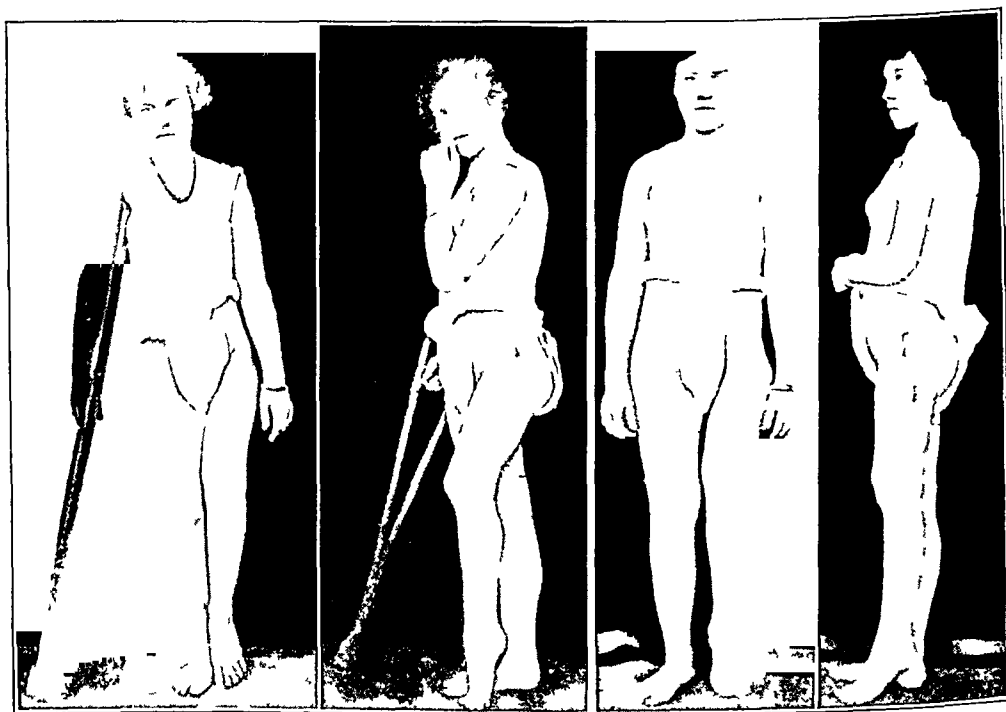


Fig 40—Subcutaneous subtrochanteric osteotomy (Adams-Gant) for pathologic dislocation from tuberculosis. Catherine Quinn, aged 18, 1914. Poor result, reconstruction operation done one year later.

if the neck cannot be made sufficiently long to secure good stability (as is often the case) a root of bone should be turned down over it. If I had employed this adjuvant for deepening the acetabulum in certain cases I am sure that relaxation would not have occurred.

*Transfer of Tensor Fasciae Femoris*—I employed transfer of tensor fasciae femoris first in 1911 soon after Davis described it. An incision about 10 or 12 cm long is made obliquely downward and forward over the subcutaneous surface of the great trochanter while the

limb is held in extreme internal rotation, the fascia lata being exposed throughout the length of the incision. The femur is then allowed to fall into extreme external rotation, thus bringing into the field of operation the lower portion of the tensor fasciae. The anterior and posterior borders of this muscle are then identified (fig 20), and the insertion of the muscle into the fascia lata is divided below the lowest muscular fibers, the muscle with its attached tendon, is cautiously dissected upward, great care being taken not to injure the nerve supply which enters from its posterior border about half way between the crest of the ilium and the great trochanter (fig 21). A longitudinal slit is then



A

B

Fig 41—Reconstruction of the left hip for tuberculosis, with sinuses. Hilda Nauyokat, 16. *A*, before operation, *B*, after operation.

made through the fascia lata over the great trochanter, and the freed tensor fasciae is pulled through this slit from its deep surface outward (fig 22). Then, while the femur is held so that the toes point directly forward, the transplanted muscle (under some tension) is sutured to the subcutaneous surface of the great trochanter. In children the trochanter is cartilaginous, and an ordinary fascia needle penetrates it easily even up to the age of 15 or 16. Finally, the free end of the tensor fasciae, protruding from the slit in the fascia lata, is turned forward and sutured securely to the band of fascia lata (iliotibial band) beneath which it has been previously passed. The skin is then closed,

and the limb is dressed in plaster of paris in the position of internal rotation and slight abduction. The plaster cast is removed in six or eight weeks, and the patient is allowed to use the limb (fig 23). Usually there is additional paralysis in the foot or leg and of course apparatus may be required for this.

#### RESULTS OF OPERATIONS ON THE HIP JOINT

*Arthrodesis*—Six operations were performed. The first and third were done by Albee's original method (1908), the second, by the removal of articular cartilage, the fourth with bone pegs and the fifth and sixth with Lambotte screws.



Fig 42—Same patient as in figure 41, roentgenogram four and one half years after operation.

CASE 1 (1913)—Abel, a woman, aged 43, was operated on for Charcot hip. The patient became maniacal soon after operation (syphilitic cerebritis) and was transferred to a hospital for the insane. Ankylosis did not result.

CASE 2 (1917)—Whipple, a boy aged 16 (same patient as in case 4) had a flail-hip resulting from anterior poliomyelitis. The head and acetabulum were denuded of cartilage. The result was no ankylosis.

CASE 3 (1920)—Mallon, a woman aged 45, was operated on, according to Albee's original method for hypertrophic arthritis. She was traced for eight years, and the following conditions were noted: slight limp, no pain, she led a normal life. The hip was stiff.

CASE 4 (1920)—In Whipple, a man aged 20 (same patient as in case 2) there was a failure of the previous operation. The bone pegs were made to transfuse the femur and to enter the pelvis. The result after nine years, was the hip was ankylosed but still required apparatus for residual paralysis.



CASE 5 (1922) —Heckler, a man, aged 20, had a flail-hip from anterior poliomyelitis, complicated by recent subcapital fracture of the neck of the femur. Fixation was done by one Lambotte screw, through both fragments into the pelvis. The result, after six years, was hip stable, flexion to 150 degrees, full extension, he could move the thigh by moving the pelvis.

CASE 6 (1927) —Thomas, a boy, aged 13, had a flail-hip from anterior poliomyelitis. Fixation was done by two Lambotte screws. The result, after two years, was bony ankylosis, he was able to move the thigh by the pelvic muscles (fig 24 *A* and *B*).

*Arthroplasty* —Four of my eight operations were failures, resulting in ankylosis (three) or pathologic dislocation (one), and four successes, three of them very successful, and one moderately so.

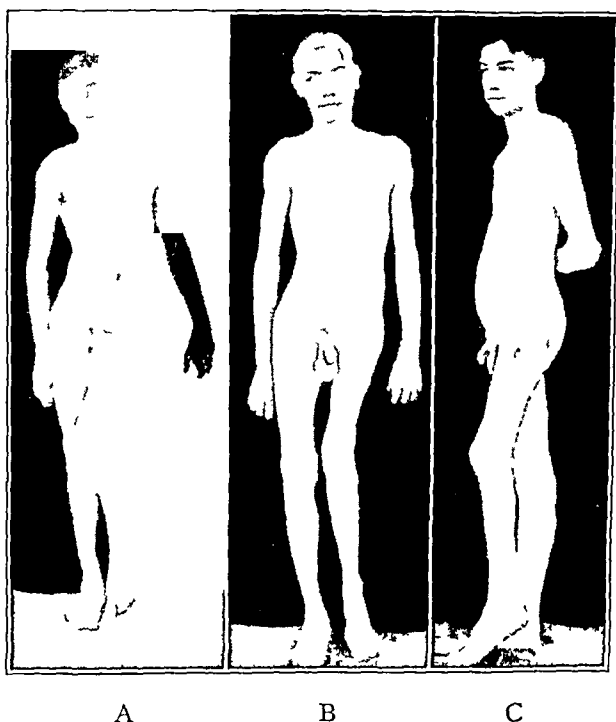


Fig 43—Reconstruction of the left hip for tuberculosis, with sinuses. Raymond Dietz, aged 16. *A*, before operation, *B* and *C*, five months after operation. See figure 44.

CASE 1 (1915) —Hall, a boy, aged 19, had gonococcic ankylosis of the left hip for over one year, there was no destruction of bone or deformity. The last note, one year after operation, was he still used a cane on the street, but went upstairs leg over leg, there was flexion to 110 degrees also full extension and normal rotation. Abduction was 75 per cent of normal. He did not limp, the hip felt a little weak. A very good result obtained (fig 25).

CASE 2 (1915) —Shollev, a girl, aged 13, had a pathologic dislocation of the left hip, following multiple arthritis (not tuberculous). The result was fibrous ankylosis (see case 4).

CASE 3 (1916) —Shollev, a girl, aged 13, had a bony ankylosis of the right hip (100 degrees flexion) following multiple arthritis. The result was bony ankylosis.

CASE 4 (1920) —Shollev, a girl, aged 18, presented a fibrous ankylosis of the left hip following an attempt at arthroplasty five years previously (case 2). A free flap of fascia lata was used at the second operation. The result was a pathologic dislocation.

CASE 5 (1921) —Shollev, a girl, aged 19, had bony ankylosis of the right hip following an attempt at arthroplasty five years previously. A free flap of fascia lata was used at the second operation. The result was gangrene of the foot from the use of adhesive plaster extension apparatus, amputation of the leg was performed and resulted in ankylosis of the hip.

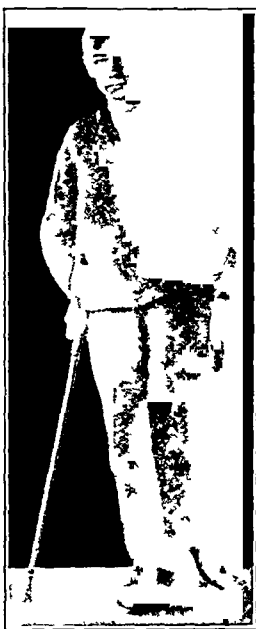


Fig. 44 —Same patient as in figure 43, eighteen months after operation. Excellent stable limb. Death from pulmonary tuberculosis three years after operation.

As a result of the second, third, fourth and fifth operations, the patient in January, 1929, fourteen years after the first operation, wore an artificial leg on the right and used a crutch when on the street. She stood all day at work. The right hip was in good position with bony ankylosis, the left hip was in pathologic dislocation and rather unstable.

CASE 6 (1915) —Davenport, a girl, aged 16, had bony ankylosis of the right hip in flexion and adduction as a result of osteomyelitis six years previously, the sinuses had been closed for six months (fig. 26). A culture from the granulation tissue at operation showed staphylococcus. The patient was traced for two years, she showed no symptoms and fair motion, she had a perfectly useful limb and scarcely limped, she wore a high-soled shoe (fig. 27).

CASE 7 (1917) —Lamb, a man, aged 22, had a pathologic dislocation following acute polyarthritis one year previously. The results (four years) were no symp-

toms, a shortening of 4 cm, flexion of 90 degrees, extension normal, abduction of 10 degrees, adduction normal, rotation outward normal and rotation inward only to the midline (fig 28)

CASE 8 (1920) —Bailey, a woman, aged 22, had bony ankylosis of the left hip in adduction, from metastatic (gonococcic?) arthritis, the duration of the condition was eight months. There was no destruction of bone. The result (nine years) was she used a light "ornamental" cane for eight years (on the street only) and no cane for the last year. There were no symptoms. Other results were flexion to 90 degrees, full extension, abduction 20 degrees, and free rotation (figs 6, 7 and 29)

*Bone Pegs* —Five operations were performed for nonunion of neck of the femur



Fig 45—Reconstruction of the left hip for tuberculosis with sinuses. Arthur Saunders, aged 17, in 1917, before operation

CASE 1 (1913) —Carrlidge, a man, aged 30, for seven months had walked only with crutches. There was disability for more than eight months after the operation. There was a fracture of transplant five months after the operation. Solid union and good range of motion resulted.

CASE 2 (1915) —Kelly, a man, aged 42, whose condition was of eleven months' duration, walked only with crutches. He was traced for eight months, with the following observations: he walked with a cane, the hip was stable, a shortening of 5.5 cm was present. Motion was limited in all directions.

CASE 3 (1915) —Baehr, a man, aged 52, whose condition was of twelve months' duration, used crutches until three months before the operation, then a

cane. He was traced for eighteen months, motion was good, and the hip was stable (figs 30, 31 and 32), he used a cane for one year after the operation. He worked all day.

CASE 4 (1919)—Smith, a woman, aged 58, for nine months had walked only with crutches. There was disability after operation for about one year. A good result was observed four years after operation, for she used no crutch or cane and there was practically no limp.

CASE 5 (1919)—Lawler, a woman, aged 50, had a condition of two and a half months' duration. There was disability after operation for about two years. The result, ten years after operation, was hip stable, flexion to right angle.



Fig 46—Same patient as in figure 45, three years after operation. He was active on the stable limb for eight years after operation, then was disabled by pulmonary tuberculosis, from which he died ten and one-half years after operation. See also figure 47, *A* and *B*.

abduction 30 degrees, rotation almost normal and 5 cm shortening. She used a cane on the street. This was a fair result.

*Bone Implants*—A case of fibrous osteitis of the trochanters and neck occurred in a woman named England. She was disabled by pain and limp.

CASE 1 (1922)—A woman aged 21 after seven years had no limp or disability. The roentgen rays showed the bone still thickened, but nearly normal.

*Capsulorrhaphy*—Three operations were performed for recurrent (habitual) paralytic dislocation of the hip

CASE 1 (1913)—In Reese, a boy, aged 5 years, there was no recurrence, the hip was stable. Death occurred from intercurrent disease sixteen months after operation

CASE 2 (1916)—Williams, girl, aged 17, operated on for recurrent paralytic dislocation of the hip, did not experience a recurrence. The hip was stable one year later

CASE 3 (1920)—Braley, a boy, aged 11, operated on for recurrent paralytic dislocation of the hip, had no recurrence. The hip was stable seven years later

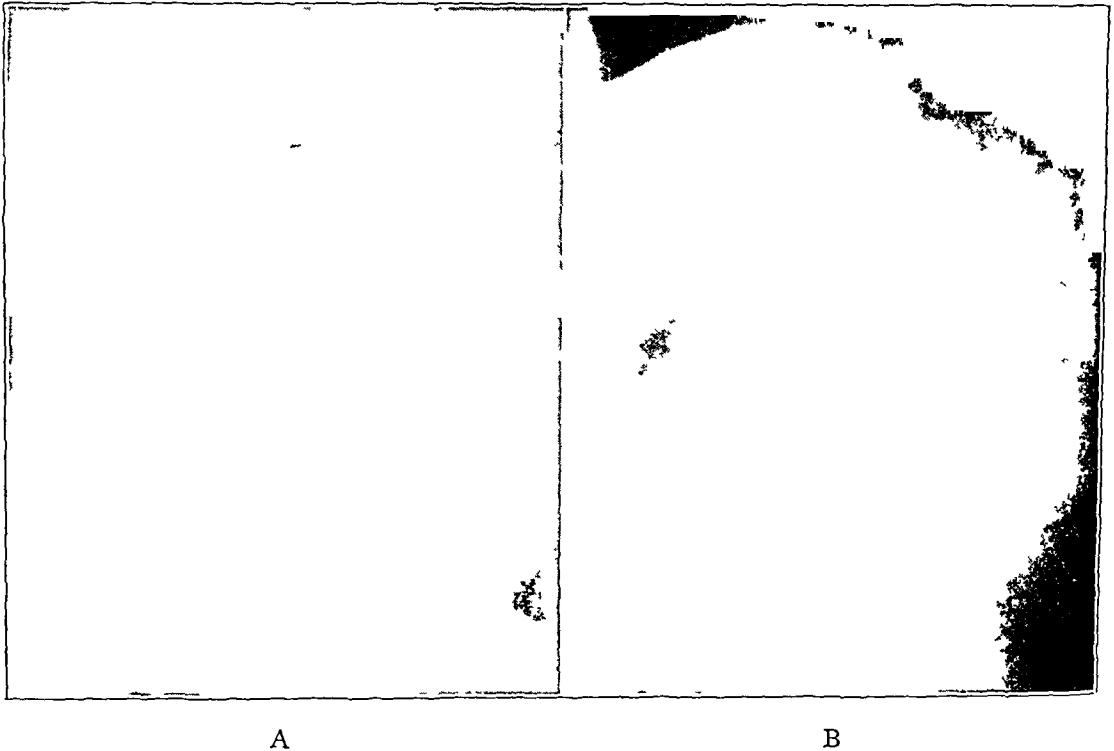


Fig 47—Same as figure 45 and 46. *A*, pathologic dislocation from tuberculosis in 1917, before operation. *B*, three years after operation

#### *Excision*—*A* For Nonunion (Three Cases)

CASE 1 (1925)—Smith, a woman, aged 64, for four years walked only with one crutch. She went home about ten days after operation. She was traced for four years. There was a shortening of 2.5 cm, she did not have pain, and she walked without support doing her own housework. This was a good result

CASE 2 (1926)—Welsh, a man, aged 64, for ten months walked only with crutches, there was much pain. He was traced for three years. He walked fairly well with a cane and he was perfectly satisfied with his improvement since the operation. He worked as a night watchman. This was a fair result

CASE 3 (1927)—Litwinski, aged 46, had poor renal function and had been disabled for more than two years. The patient walked only with crutches and

experienced much pain. The patient was traced for two years, at which time he could walk without support. He was considered a malingerer. This was a fair result.

### B For Malunion (One Case)

CASE 1 (1921) —Brzezinski, a man, aged 45, had a condition of three years' duration. He was traced for eight months. The result was good.

### C For Acute Osteomyelitis (Six Cases)

CASE 1 (1914) —In Vivian, a boy, aged 15, the trochanteric region was guttered five days after onset, the hip was excised eighteen days later. One year later, there was no deformity except shortening, but he had a dreadful limp, the

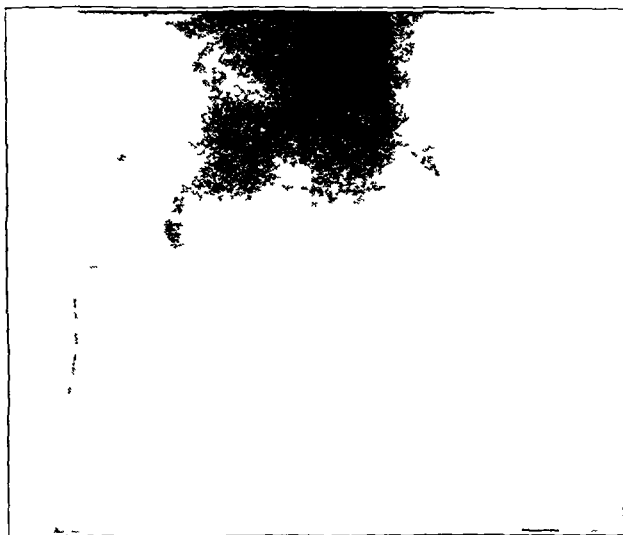


Fig. 48—Pathologic dislocation of the left hip from osteomyelitis in infancy. Lawrence Scheff, aged 5 years, in 1919.

femur was sliding up and down on the pelvis for about 5 cm (see case 1, Reconstruction for Pathologic Dislocation).

CASE 2 (1915) —King, a boy, aged 9 years, had an acute condition. Death occurred, from the continuance of sepsis, nine hours after operation.

CASE 3 (1919) —Vedro, a boy, aged 12, had an abscess in the adductor region drained two weeks before excision of the hip and one week after the onset of the disease (fig. 9). The great trochanter and neck of the femur were reformed after excision (figs. 10 and 11). He was traced for ten years, and at the end of that time he showed a very slight limp and a shortening of 1 cm, the hip was stable, there was good function, and the sinuses finally healed about four years after operation. This was a good result (fig. 12).

CASE 4 (1925) —In Freund, a boy, aged 17, the femur was drained about four months previously for acute osteomyelitis, a pathologic fracture occurred before excision of the upper end of the femur was done. He was traced for four years, at which time the hip had been healed for two years, the hip was stable, there was flexion to 90 degrees and full extension, there was a shortening of 65 cm and a moderate limp. He did not use a cane and could walk for two

hours at a stretch, there was no disability. The result was good, but the femur was not in the acetabulum (figs 33 and 34).

CASE 5 (1928) —In Schrawder, a girl, aged 9 years, the right hip was drained about six months previously for acute osteomyelitis. There was bilateral pathologic dislocation of the hips, a sinus on the right with necrosis of the head and no sinus on the left ("silent osteomyelitis"). The dislocation on the right was reduced by Buck's extension, then the necrotic head was excised. Later reconstruction was done on the left hip. As a result, the right hip was stable, a stump of the neck was in the acetabulum, and the sinus was healed.

CASE 6 (1929) —In Ashton, a boy, aged 7 years, the left femur was guttered for acute osteomyelitis fifteen days after onset, excision of the hip was done

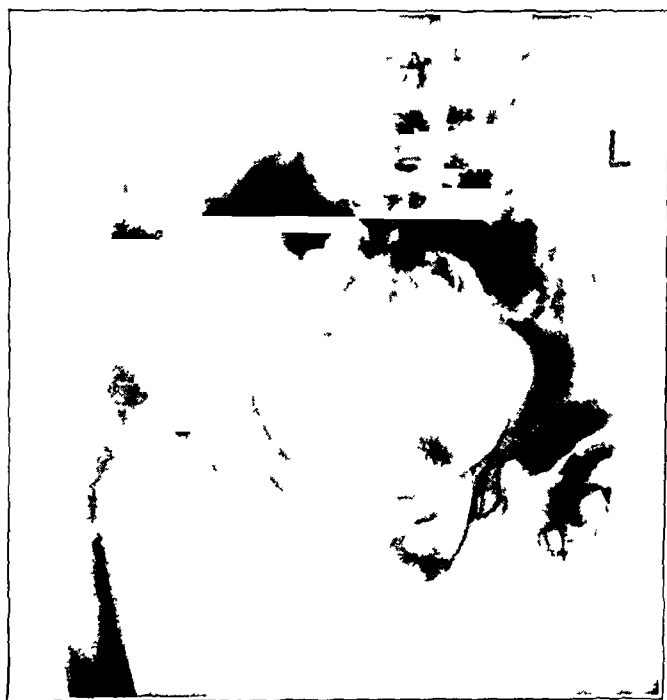


Fig 49—Same as figure 48, seven years after operation. See also figure 50.

eighteen days after the first operation for persisting sepsis. Recovery occurred, but the patient is still under treatment.

*D For Tuberculosis (Seven Cases)* One death from tuberculous meningitis occurred two months after operation.

CASE 1 (1906) —Ellingson, a boy, aged 6 years, had an operation for sinuses and secondary infection. He was traced longer than two years, at which time he was using crutches, there was no sinus.

CASE 2 (1907) —Brennan, a boy, aged 6 years, had an operation for sinuses and secondary infection. He did well for six weeks. Tuberculous meningitis and death occurred two months after operation.

CASE 3 (1914) —Swartz, a boy, aged 9 years, was operated on for sinuses and secondary infection. He lived for more than three years after operation, but the sinuses never closed, death occurred from amyloid disease.

CASE 4 (1915)—In Shafer, a man, aged 41, the pelvic bones were diseased, there were sinuses and secondary infection. The sinuses never healed, death from pulmonary tuberculosis occurred in less than two years.

CASE 5 (1919)—Fleet, a man, aged 29, had a sinus for one month before operation. There was disability for about one year after operation. He used a cane for eighteen months or two years. Eighteen months after operation he weighed from 185 to 190 pounds (83.9 to 86.2 Kg) (height 5 feet 6 inches [167.6 cm]). He was traced for nine and a half years at which time he worked half time, sitting down, the weight was stationary (from 185 to 190 pounds), the hip was stable, he went up and down stairs leg over leg, he did not use a cane, he showed good station, and had a moderate limp. The hip flexed to 100 degrees.

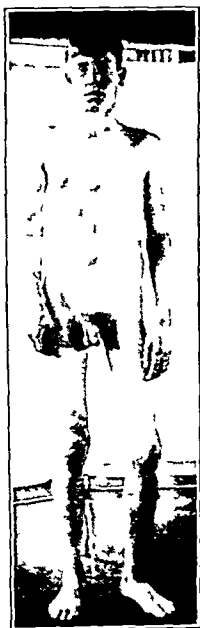


Figure 50



Figure 51

Fig 50—Same as figures 48 and 49 seven years after reconstruction for pathologic dislocation from osteomyelitis in infancy. ankylosis in good position.

Fig 51—Paralytic outward rotation of the left lower extremity, six years after transfer of the tensor fasciae to the great trochanter. Leonard Coester aged 13 (1921).

and extended to 180 degrees, abduction was 30 degrees, rotation was fair (figs 13 and 14). The result was good.

CASE 6 (1921)—Jarrett, a woman, aged 36, had ankylosis, with pain and deformity. She was traced for seven years, a sinus persisted until five years after operation, she did her regular work, there was no disability, except a limp and shortening of the leg. The result was good.

CASE 7 (1926)—Seeberger, a boy, aged 11, had sinuses with secondary infection. After excision he was sent to the Home for Consumptives at Chestnut Hill, Philadelphia, for two years (heliotherapy). He was traced for more than three years, all the lesions had been healed for one year, he used a brace and crutches, he was still under treatment.



*Open Reduction*—Thirteen operations were performed, one death from shock resulted

CASE 1 (1908)—Passoloqui, a girl, aged  $8\frac{1}{2}$  years, was traced for one year, the dislocation recurred, but the hip was more stable. She was much improved.

CASE 2 (1913)—Strassbaugh, a girl, aged  $11\frac{1}{2}$ , was traced for sixteen years, the dislocation recurred promptly, but since five years after operation she had led an ordinary life. She sometimes had pain in the hip, and she was unable to walk for a time. She was 28 at the time this article was written.

CASE 3 (1915)—In Kisch, a girl, aged 3 years, the dislocation was recurrent after a bloodless reduction. She was traced for fourteen years, at which time she had a scarcely visible limp and normal movements, there was no pain or disability, the head was in a good false acetabulum on each side of the pelvis.

CASE 4 (1920)—Pipps, a boy, aged 11, was not traced.

CASE 5 (1920)—Di Girolomo, a girl, aged 11, was traced for two years, reduction was maintained, there was a notable limp but no pain, the thigh was in external rotation of 45 degrees, there was full extension, with flexion to 150 degrees, no abduction or adduction was present.

CASE 6 (1920)—Yeoman, a girl, aged 8 years, had an operation on the right hip. The dislocation recurred (case 8).

CASE 7 (1921)—Yeoman, a girl, aged 9 years, had an operation on the left hip. She was traced for eight years, at which time reduction was maintained, there was no disability.

CASE 8 (1922)—Yeoman, a girl, aged 10 years, had a second open reduction of the right hip, the dislocation recurred. She was traced for seven years, at which time there was a moderate limp, but no disability.

CASE 9 (1921)—Clark, a boy, aged 6 years, was traced for two and a half years, the hip was nearly stiff and in good position, reduction was maintained.

CASE 10 (1921)—In Bauer, a girl, aged 8 years, the dislocation recurred promptly, a reconstruction operation was done one month later (see case 1, reconstruction for congenital dislocation).

CASE 11 (1922)—In Drenner, a girl, aged 5 years, the condition recurred nine months later. She was traced for seven years, there was still a slight limp and some pain at times, the hip was stable, there was no disability (aged 12).

CASE 12 (1922)—Dovas, a girl, aged 9 years, was not traced.

CASE 13 (1923)—In Wiley, a girl, aged 13, death occurred from shock five hours after operation, at which time reduction was secured only after much manipulation.

*Summary*—There were seven recurrences of the dislocation among ten traced cases, two were not traced, and one death occurred from shock. In two of the patients in whom reduction was maintained, the hips are nearly stiff, the operations having been done when the patients were 11 and 6 years respectively, only in the patient who was operated on at the age of 3 years has normal motion been preserved, and yet the head is in a false acetabulum. In five of the seven recurrences the hips were fairly stable, and the patients were in considerably better condition than before the operation.

From the aforementioned very poor results of the operation in my hands, it is natural that in most cases I should prefer the reconstruction method. Even in the cases in which reduction into the true acetabulum is comparatively easy to obtain, stable reduction is not maintained unless (a) the acetabulum is deepened considerably or (b) a bony roof is turned down over it from above. In the former case a stiff joint is the usual result, while the latter plan can often be used to greater advantage in connection with a false acetabulum (already existing, or made by the surgeon) than with the original shallow and deformed joint socket.

*Osteoclasia* (Anzoletti) —As I employed this method of correcting rachitic coxa vara in only one patient (Plummer, a boy, aged 3 years, both hips), it is manifestly impossible for me to conclude anything definite as to its results. All I can say is that in this patient the correction of the deformity was adequate and satisfactory, though the necks were not restored completely to their normal angle with the shafts.

*Osteotomy* —Fifteen operations were performed, with one death (on the operating table, perhaps from the anesthetic, ether).

CASE 5 (following) —In a negro girl, aged 12 years, the operation (cuneiform osteotomy of the neck for bony ankylosis in adduction) was easy to perform, it had been completed, and the plaster of paris dressing was being applied. The child had been breathing poorly for about five minutes, when she suddenly stopped breathing and could not be revived. Artificial respiration brought a few gasps, but there was no pulse and there were no heart sounds, the epigastrium was opened and subdiaphragmatic massage of the heart was begun, but the heart was apparently contracted in systole, and no pulsations could be made to return. The autopsy showed "status lymphaticus"—enlarged thymus, enlarged spleen and enlarged bronchial and mesenteric lymph nodes, the heart was normal. The family said that several times the child had been "nearly frightened to death" by trivial occurrences.

#### A Osteotomy Through the Neck (Open) 1 "Slipped Epiphysis" (Three Cases)

CASES 1, 2 AND 3 —(1916) Dilkes, a girl, aged 13, (1926) Saloner, a boy, aged 14 (figs 35 and 36), and (1928) Povernick, a boy, aged 13. The three patients were obese, and cases 1 and 3 were of the hypopituitary type. The patients were treated by open cuneiform osteotomy through the neck, an excellent result was obtained in two, but the third patient (Povernick) was still under treatment, and was suing for damages for the original injury, the operation promised to give an excellent result.

#### 2 Coxa Vara (One Case)

CASE 4 (1921) —Sonak, a boy, aged 10, had a condition that probably dated from a fracture of the neck in infancy. He was treated by open cuneiform osteotomy through the neck. He was traced for eight years, there was an excellent result. He was fond of long "hikes" swimming and camping; there was always a slight limp. He was killed at the age of 18 in a railroad accident.

### 3 Bony Ankylosis from Osteomyelitis (Two Cases)

CASE 5 (1922) —In Ford, a girl, aged 12, death occurred on the operating table, the case was referred to previously

CASE 6 (1928) —Hackett, a boy, aged 19, was operated on because the limb was in external rotation. He was treated by open curvilinear osteotomy, the operation gave an excellent result

### B Osteotomy Below the Trochanters 1 Open Osteotomy (Four Cases)

CASES 1, 2, 3 AND 4—(1928) Santangelo, a boy, aged 7 years, was operated on for coxa vara, probably from fracture of the neck in infancy. Three operations were performed to overcome outward rotation of the femur: (a) (1914) ankylosis from osteomyelitis in Wenick, a girl, aged 14 (fig 37), (b) (1920) deformity from infantile paralysis in Bitto, a boy, aged 11, and (c) (1925) deformity (abduction and external rotation) following bloodless reduction of congenital dislocation four years previously in Remley, a girl, aged 13 (fig 38). Excellent results were obtained in all four cases

### 2 Subcutaneous Osteotomy (Adams-Gant Method) (Five Cases of Tuberculosis)

CASES 5, 6, 7 AND 8—There was apparently bony ankylosis in these four patients: (1911) Devine, a girl, aged 13, (1916) Dolan, a girl, aged 13, (1924) Walker, a girl, aged 12, and (1929) Shaffer, a girl, aged 16 (fig 39). Excellent results were obtained in all

CASE 9—There was a flexion-adduction deformity, without ankylosis (1914) in Quinn, a girl, aged 17, a poor result obtained, the lower fragment slipping past the upper into the adductor region (fig 40). She was later treated by reconstruction (case 3, under reconstruction for tuberculosis)

*Reconstruction* —Twenty-seven operations were performed, 1 death from uremia resulting four days after operation (1927, Hensel, a man, aged 59, utterly incapacitated by hypertrophic arthritis)

### A Reconstruction for Tuberculosis (Twelve Operations)

CASE 1 (1914) —Nauyokat, a girl, aged 16, presented pathologic dislocation with sinuses. She was traced longer than five years, at which time there was an excellent stable limb (figs 41 and 42)

CASE 2 (1914) —Dietz, a boy, aged 16, had a pathologic dislocation, with a sinus. After operation there was an excellent stable limb (figs 43 and 44). He died after three years of pulmonary tuberculosis

CASE 3 (1915) —Quinn, a girl, aged 19, had fibrous ankylosis in bad position (case 9 reported under subcutaneous osteotomy below the trochanters), she experienced recurrently disability through pain, there was no sinus. She was traced for thirteen years. There was an excellent stable limb, she did all her own housework, even scrubbing the floor on her knees

CASE 4 (1917) —Saunders, a boy, aged 17, had pathologic dislocation with sinuses. He was traced for ten and a half years, until death occurred from pulmonary tuberculosis. He was active on the stable limb for eight years after operation (figs 45, 46 and 47)

CASE 5 (1917) —Fitzpatrick, a boy, aged 17, was operated on for pathologic dislocation, there was a healed sinus. He was traced for four years, and was still in good health, he used a cane even in the house, there was never any pain.

CASE 6 (1919) —Rakowsky, a boy, aged 17, had a pathologic dislocation, with a sinus recently healed. The result of the operation was good. He was traced for two years when death occurred from an unknown cause.

CASE 7 (1922) —Shaffer, a girl, aged 9 years, was operated on for pathologic dislocation, there was no sinus. She was traced for seven years. There was a bony ankylosis in flexion of 135 degrees. There was excellent weight-bearing and no pain, but an abominable limp. Adams-Gant osteotomy was done in 1929.

CASE 8 (1922) —McMahon, a girl, aged 15, had a pathologic dislocation, but no sinus. She was traced for seven years. The limb was useful, but not very stable, there was fair motion, she had to bend the knee to reach the shoe. She worked full time, sitting down. Pain and stiffness were present in wet weather. No crutch or cane was used.

CASE 9 (1924) —Moyer, a man, aged 29, had a fibrous ankylosis in bad position, with sinuses, he walked only with the aid of crutches. He was traced for five years, he wrote, "I am as fat as a pig." The sinuses had been healed for two years and the limb was stable.

CASE 10 (1926) —Rust, a man, aged 21, had a fibrous ankylosis in bad position, with pain, there was no sinus. Death occurred after three years, he was improved for one year, then was an invalid. The sinus persisted, and he had amyloid kidneys.

CASE 11 (1926) —Blank, a boy, aged 15, had a fibrous ankylosis in bad position. He was traced for three years. He did well at first, then developed sacroiliac tuberculosis and, later, tuberculosis of the left shoulder joint. In 1929, he was steadily improving, the shoulder was healed, the sinuses at the hip were still open, he was up and about on crutches and was "fine and strong."

CASE 12 (1929) —Ozykowski, a boy, aged 9 years, was operated on for pathologic dislocation with sinus. He was still under treatment.

All of these twelve patients, varying in age from 9 to 29, were improved at least temporarily, and of nine operated on six were still leading active and useful lives, walking on the limb, more than five years after operation, though one of these died of pulmonary tuberculosis more than ten years after operation. The patients in cases 2 and 4, which are elaborated, show what may be accomplished, even if the improvement is only temporary.

CASE 2 —Raymond Dietz, aged 16, had never borne any weight on the diseased limb, having developed the disease as an infant. His hip had been treated by excision about eight years previously, leaving a sinus which was sometimes moist. His life had been spent in institutions as a patient. He came under my care at the Episcopal Hospital where he was a candidate for the Harrison Memorial House for Incurables (figs 43 and 44). His limb showed 135 cm actual shortening. After reconstruction of the hip, he was able to walk well with a cane and a high shoe (fig 44). He left the hospital and worked for his living for more than two years. He then returned with active pulmonary tuberculosis, and died three years after operation. Perhaps if I had not "cured" him temporarily he would be still living in the incurable ward.

CASE 4—Arthur Saunders, aged 17, entered the Episcopal Hospital emaciated, in pain, with a discharging sinus and a cold abscess (fig 45) After reconstruction, he led a normal life for eight years, gaining 18 pounds (8.2 Kg) in the first two years (figs 46 and 47) After eight years he developed active pulmonary lesions, from which he died ten and a half years after operation

### B Reconstruction for Pathologic Dislocation from Osteomyelitis (Six Operations)

CASE 1 (1915)—In Vivian, a boy, aged 15, about one year after excision for acute osteomyelitis, reconstruction was done because of marked instability and abominable limp He was traced for nine years He wore a high shoe (12 cm) and limped, but had no disability of any kind at any time, he added "not even pain in damp weather" There was fair motion

CASE 2 (1921)—Graham, a girl, aged 9 years, had the condition since infancy She was traced for ten months, walking was much improved

CASE 3 (1922)—Scheff, a boy, aged 5 years, had the condition since infancy He was traced for seven years, at which time there was bony (?) ankylosis in good position, there was some pain in damp weather There was scarcely any limp (figs 48, 49 and 50)

CASE 4 (1923)—Wenskis, a girl, aged 19, had the condition for twelve years, she tired after walking three or four squares She was traced for ten months There were bony ankylosis in good position, considerable limp and some pain in damp weather, she felt much better after the operation

CASE 5 (1924)—Lebender, a boy, aged 9 years, had the condition since the age of 6 weeks He was traced for five years He thought he "could not be improved", there was no disability (now 14 years of age), all motions were normal except abduction, only to 30 degrees, and there was no hyperextension A marked limp was present, with a shortening of 6 cm, the trochanter slid up and down on the pelvis about 2 cm He walked on his toes

CASE 6 (1928)—Schrawder, a girl, aged 9 years, had the disease for about nine months She was traced for four months The hip was more stable, but the end of the femur was not in the acetabulum

### C Reconstruction for Congenital Dislocation (Four Operations)

CASE 1 (1921)—Bauer, a girl, aged 8 years, was operated on for recurrence after open reduction five weeks previously She was traced for seven months The hip was stable in the false acetabulum

CASE 2 (1925)—Fisher, a girl, aged 12, had a dislocation of the left hip She was traced for four years, the hip was stable in the false acetabulum, and there was a fair range of motion (case 4)

CASE 3 (1926)—Stellone, a girl, aged 17, was traced for three years The hip was stable in the false acetabulum, there were fair motion, a shortening of the leg of 1.5 cm, no pain in the hip and a moderate limp (fig 15)

CASE 4 (1927)—Fisher, a girl, aged 14, had an operation on the right hip She was traced for two years The hip was stable in the false acetabulum, there was a fair range of motion (case 2)

### D Reconstruction for Slipped Epiphysis (One Operation)

CASE 1 (1928)—Zeller a boy, aged 16, was traced for eight months There was no pain some stiffness after sitting and a considerable limp were present He

said that he was "much" better than before the operation. There was good position and the hip was stable in the old acetabulum, a fair range of motion was maintained.

### E Reconstruction for Nonunion of the Neck (Two Operations)

CASE 1 (1924) —Eichelberger, a woman, aged 31, had nonunion of the neck for five months. She was traced for five years, she had not done heavy work for one year, she now climbed chairs and even fences without trouble. There was flexion to 110 degrees, extension to 180 degrees, rotation was normal, toes forward. There was a slight limp and some stiffness in damp weather. The hip was stable in the old acetabulum. There was a shortening of 1 cm (fig 19).

CASE 2 (1927) —Donovan, a woman, aged 40, had a nonunion of the neck for three months. She was traced for eighteen months, she used a cane and had a moderate limp, she began ordinary housework (cleaning and scrubbing) about four months after operation. There was a shortening of about 2.5 cm, the hip was stable. Flexion was 120 degrees, extension, 180 degrees, rotation was limited, toes forward.

### F Reconstruction for Dystrophic Arthritis (Two Operations, One Death)

CASE 1 (1927) —Hensel, a man, aged 59, was entirely disabled from hypertrophic arthritis. Death occurred from uremia four days after operation.

CASE 2 (1928) —Chanudet, a woman, aged 32, was entirely disabled from atrophic arthritis of the hip and knee. She was traced for one year, at which time she was able to be around a little with a knee brace and cane. There was no pain in the hip, and she had a fair range of motion, the joint was stable.

### *Transfer of Tensor Fasciae Femoris*—Six operations were performed for paralytic outward rotation of the thigh.

CASE 1 (1911) —Foster, a girl, aged 15, after two months had active internal rotation of the hip.

CASE 2 (1913) —Simpson, a boy, aged 6 years, was traced for fourteen years, the toes pointed forward in walking, and active internal rotation was strong (fig 23).

CASE 3 (1914) —Coester, a boy, aged 7 years, was traced for six years. There was practically no control of the hip, except that when he was erect he could rotate it in and out slightly (fig 51).

CASE 4 (1914) —Gropp, a boy, aged 7 years, was traced for one year. He walked without support, the right foot (side of operation) was in marked eversion.

CASE 5 (1920) —Gaunt, a boy, aged 16, was traced for nine years, he considered himself much improved, he still used crutches for residual paralysis.

CASE 6 (1922) —Kratz, a boy, aged 12, was traced for seven years. The toes pointed forward in walking, the transplanted tensor fasciae abducted more than it internally rotated the hip.

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# SPINAL CORD INJURY\*

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The surgeon whose lot it is to care for a patient with trauma to the spinal cord needs much information concerning his patient before finally deciding on the plan of treatment, whether it is to be operative or nonoperative

If, in a case of this kind, it were possible to have a little more knowledge regarding the etiology and the pathology and the relation of the one to the other, such data would often be welcome. Was all the damage to the cord inflicted at the time of the injury, or is there still pressure from misplaced fragments causing damage to the cord? Again, just what is the pathologic condition of the cord after receiving the trauma? These questions must be answered in each case. The roentgen examination of the spinal column following the injury may be negative in results, yet there may be complete loss of function of the cord below the level of the injury. If, instead of depending on a single x-ray picture taken after the force causing the lesions has been removed, one could imagine a motion picture showing the relationship of the various vertebrae to the spinal canal and the cord therein during the time of the application of the force, it seems one could visualize what happens pathologically in many cases of "flexion" injuries of the cord. In "flexion" injuries of the spine, sometimes spoken of as "jackknifing" of the spine, the cephalic portion of the spine is approximated toward the caudal end of the spine or, in other words, the head and knees are forcibly approximated. If this force is sufficient, several conditions may result.

With the buckling of the spinal column, one vertebra may be dislocated anteriorly or laterally over its neighbor below (fig 1 A). While this is the position of dislocation, the lumen of the vertebral canal is encroached on, and the cord consequently is compressed between the laminae or between the arch of the dislocated higher vertebra and the posterior part of the body of the vertebra below (fig 2). Then, when the force causing the dislocation is released, the dislocated vertebra may return to its normal position or may remain dislocated. If the dislocation of the vertebra is reduced an x-ray picture of the end-result (fig 1 B) may give a normal appearance as far as the bony structures are concerned. However the damage to the cord has been

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done. Operation in this case, of course, is purposeless. If, however, the dislocation is not reduced when the causal force has ceased, the cord then may continue to be compressed as described. If reduction cannot be effected by nonoperative methods, then, of course, a decompression laminectomy is indicated.

Again, when the force causing flexion is great, the anterior portion of the bodies of the two adjacent vertebrae may suffer a compression

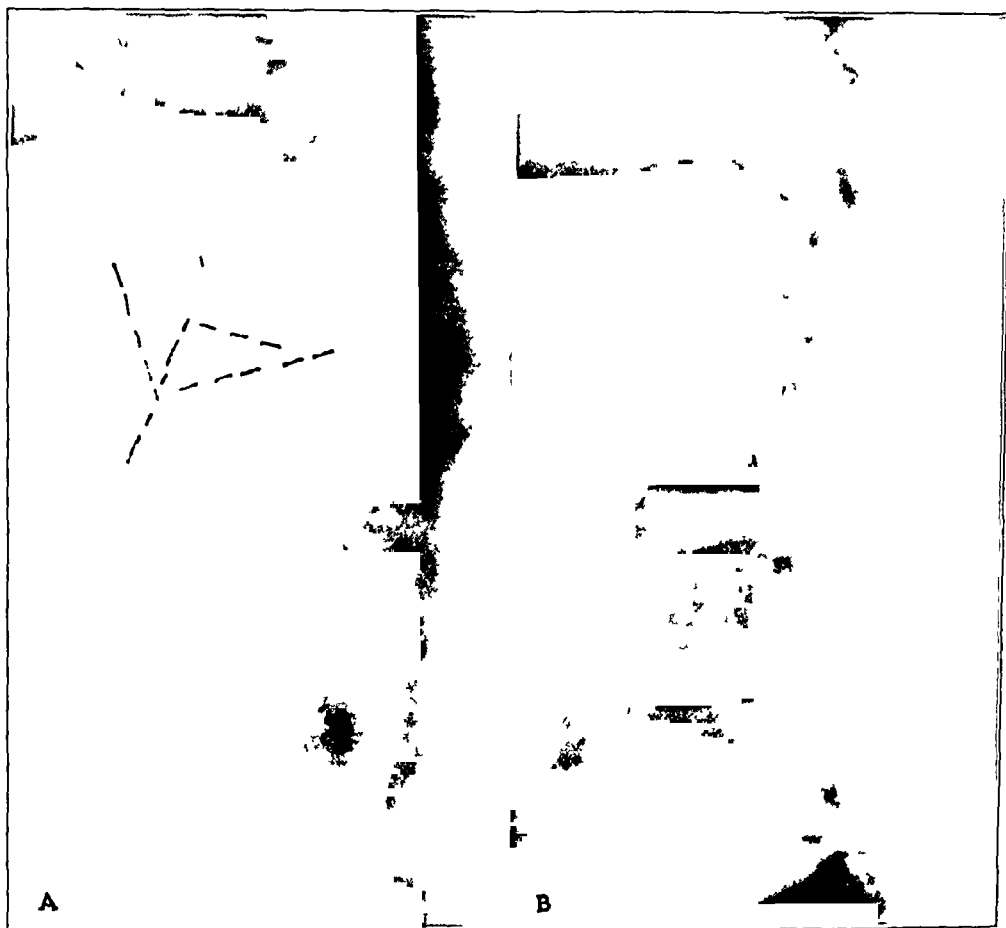


Fig 1 (case 1)—*A*, lateral dislocation of second lumbar vertebra after the application of a force sufficient to cause buckling. The picture represents the dislocation before reduction. Note the crisp, definite outlines of the bodies, showing no compression fracture, but does show a narrowing of the spinal canal.

*B*, The dislocation shown in *A* after reduction accomplished by nonoperative procedures. The reduction was made by hyperextension. Note the crisp outlines of the bodies of the vertebrae (first and second lumbar). No evidence of a compression fracture is seen. The spinal canal is restored to its normal lumen.

fracture (fig 3), and with this again a dislocation of the upper of the two vertebrae producing a fracture dislocation (fig 4). When the causal force is released the dislocation may be reduced, in this case,

in the x-ray picture, the only evidence of what has happened during the buckling is the picture of the compression fracture of the anterior portion of one or both bodies of the vertebrae involved. The damage to the cord has been done and again operative procedure is purposeless.

Another portion of this imaginary motion picture showing the buckling of the spine would be of interest. It would be the pathologic change produced in the posterior portion or arch of the vertebra by the direct action when the force is applied. This force might be a heavy



Fig 2—Anterior dislocation of fourth cervical vertebra from application of a force sufficient to cause buckling resulting in narrowing of the lumen of the spinal canal, trauma to the spinal cord and paralysis of both arms and both legs

object falling on the arches of the vertebrae causing local injury to an arch and buckling of the spine with accompanying dislocation or fracture dislocation, or the patient might fall from a height and, landing on his back, take the force of the fall on the arches of certain vertebrae.

The senior author has noted that when there is a dislocation or fracture dislocation from the buckling, the damage to the cord is inflicted at the time the force causes the greatest flexion of the spine with a simultaneous narrowing of the canal impinging on the cord and that with the release of the force reduction of the dislocation generally and restoration

of the normal outline of the lumen of the spinal canal and accordingly removal of any pressure on the cord, follow. The pathologic change suffered by the arch of the vertebra receiving the direct force is generally the prime factor in causing pressure on the cord after the primary causal force has been removed.

An x-ray picture, in anteroposterior view, taken after the injury, frequently shows, in these cases, a unilateral or bilateral fracture of the laminae of the vertebrae involved. If, in addition, one is able to note that the shadow of the bulbous portion of the spinous process is laterally displaced and is out of line with those of the vertebrae above and below, one may with a reasonable degree of assurance make a diagnosis of pressure on the cord by the depressed fractures of the arch (fig 5),

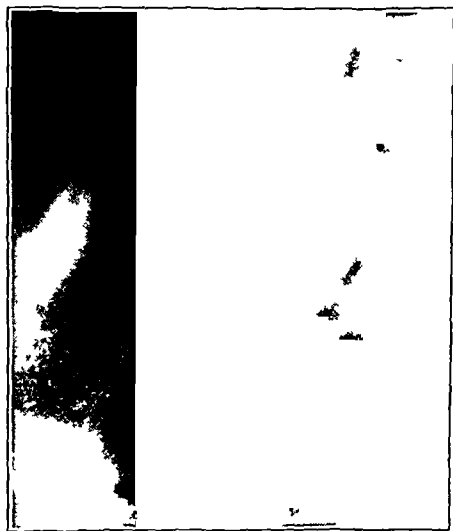


Fig 3—Compression fracture resulting from the application of a force sufficient to cause buckling

and a decompression laminectomy is indicated. Of course, the spinous process alone may be fractured and displaced laterally without a fracture of the lamina and too much importance should not be given to asymmetry of spinous processes, unless accompanied by shadows showing fractures of the laminae.

The neurologic observations in the presence of injuries of the spinal cord are of greatest importance, and the surgeon, unless he has specialized in neurologic surgery, may well consult his colleague, the neurologist.

We wish to present the history and the roentgenologic, neurologic, and postmortem observations on a patient who received an injury to the spinal cord and died as the result of the injury seventeen days later.

## REPORT OF CASE

*History*—On April 15, 1926, a structural iron worker, aged 38, fell from a scaffold, 25 or 30 feet to a cement floor. The patient, who did not lose consciousness at the time of the injury, believed that he landed on his buttocks but that his head struck a wall. He tried to get up and walk, but could not. He was taken to the hospital.

On admittance to the hospital on the fifteenth of April, the patient complained of pain in the right arm, forearm and hand and also in the interscapular region and in both hips. He further noticed numbness of both legs and hands.

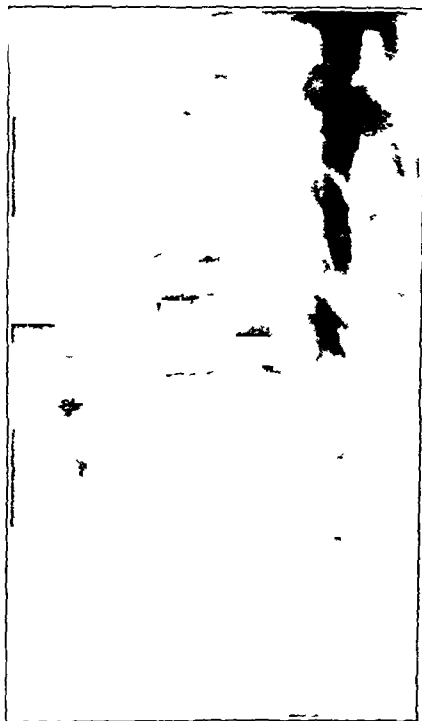


Fig 4—Compression fracture and dislocation of the eleventh and twelfth dorsal vertebrae, resulting in paralysis of both legs

*Roentgen Examination*—The roentgenogram (fig 6) showed a smearing of the intervertebral space between the sixth and seventh cervical vertebrae and a compression fracture (?) of the body of the sixth cervical vertebra.

*Physical Examination*—The patient had a wrist drop of the right wrist and he was unable to flex or extend the right wrist or the fingers of the right hand. The same was true of the fingers of the left hand. All voluntary motion of the lower extremities was lost. The active and passive movements of the neck were normal, and the cranial nerves were normal, including those controlling the size of the pupils. The respiratory movements and the excursions of the diaphragm were normal. There was moderate rigidity of the neck and also slight rigidity of abdominal muscles and priapism.

The bladder was distended, and there was no voluntary movement of the bladder or rectum. The biceps and triceps reflexes were present but the knee

jerk, the Babinski sign, and ankle clonus were absent (Later examinations showed the knee jerk to be present)

*Sensory Examination*—There was loss of pain and temperature sensations over the lower extremities and the trunk as high as the third chondrosternal junction anteriorly, and the spine of the fourth thoracic vertebra posteriorly. On the right upper extremity, there was anesthesia to pain and to temperature stimuli over the entire dorsal surface of the hand (with the exception of the thumb), the dorsal side of the forearm and the dorsal side of the upper arm as high as the insertion of the deltoid muscle. The area of anesthesia continued on the ulnar side of the dorsal surface of the arm and was continuous with the area of anesthesia on the posterior part of the trunk. On the anterior surface of the right upper extremity, the area of anesthesia was found on the ulnar side

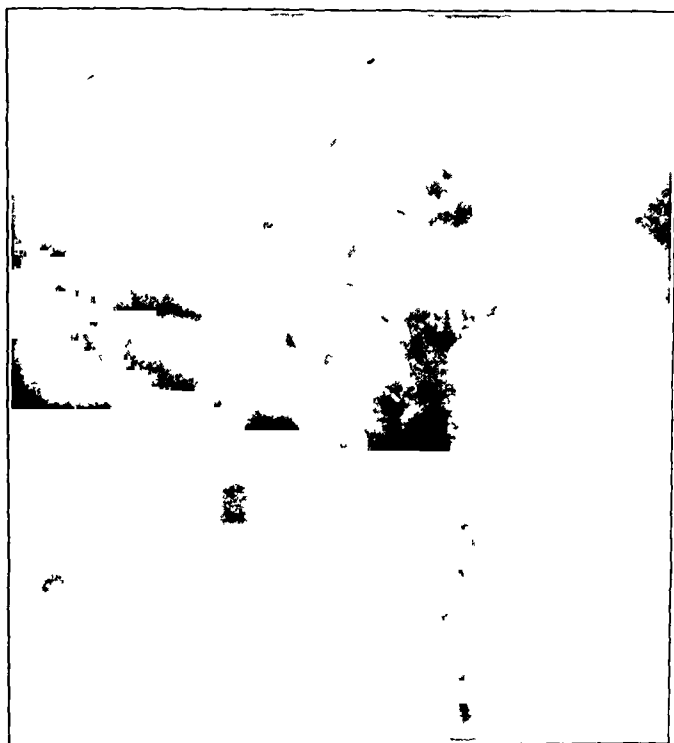


Fig 5—Fracture of the lamina and lateral displacement of the bulbous end of the spinal process of a dorsal vertebra (second thoracic) from application of a direct force. The injury caused paralysis of both legs.

including all of the hand except the thumb, the ulnar half of the forearm and a narrow strip on the ulnar side of the arm, which was continuous with the anesthetic area on the anterior part of the trunk. On the left upper extremity, the area of anesthesia to pain and to temperature was a narrow strip along the ulnar side of the extremity. Unfortunately, the left arm was not examined as carefully as the right.

Tactile sensibility (to cotton wool), position sense, and discriminatory sense were present everywhere.

The sensory and motor observations were those of a loss of voluntary movements below and including the seventh cervical segment, and of loss of pain and

temperature sensibility below and including the first thoracic segment on the left side and the eighth cervical segment on the right side (fig 7)

*General Examination*—General physical examination revealed a young white man, lying motionless in bed who was entirely conscious. There was a laceration 3 inches (7.6 cm) long in the midfrontoparietal region. Two other lacerations each one-fourth inch (0.61 cm) long, opened into this laceration. In addition, there was a laceration three-quarters of an inch (1.83 cm) in length in the left supraorbital region and another one-quarter of an inch (0.61 cm) in length on the bridge of the nose. Otherwise, the examination of the head was negative. The pupils reacted to light and in accommodation, and were normal in size. The

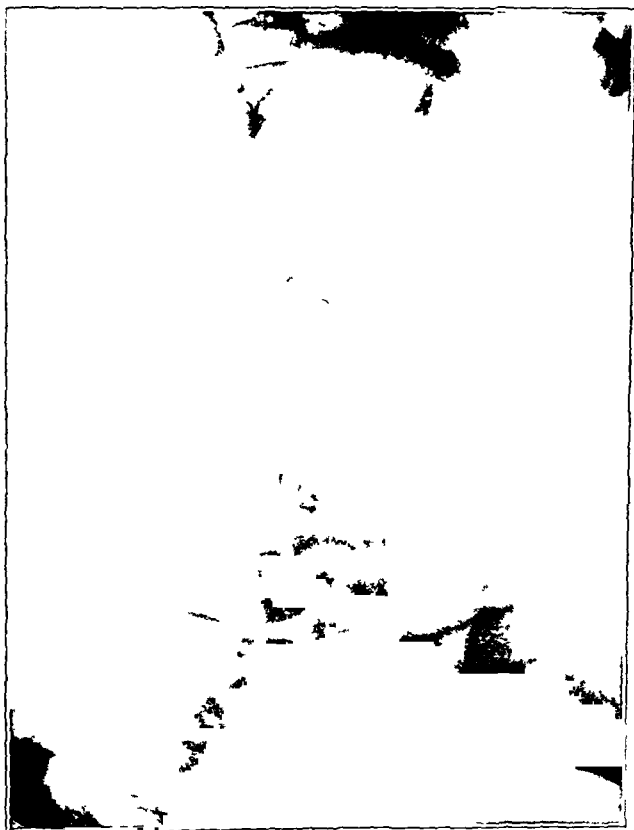


Fig 6—Compression fracture (?) of the body of the sixth cervical vertebra and a smearing of the intervertebral space between the sixth and seventh cervical vertebrae

palpebral fissures were normal. Otherwise, the examination of the eyes disclosed normal conditions. The ears, nose and mouth were normal. The throat and the chest were normal. There was a slight rigidity of the abdominal walls, but there was no tenderness. The liver, spleen and kidneys were not palpable.

*Treatment and Course of Illness*—The wounds on the head were sutured. The head of the bed was raised slightly, and a Jurek mast was applied to the patient's head with 10 pounds (4.5 Kg) of extension. Two days after the injury on the seventeenth of April, he was examined by Dr G B Hassin whose observations are appended. The Jurek-mast was removed at this time and a spinal puncture

was performed. The pressure of the spinal fluid was 8 mm of mercury. Twenty cubic centimeters of fluid were removed. The fluid contained some blood.

On the twenty-first, another spinal puncture showed the same pressure. There was less blood in the spinal fluid, and again 20 cc was removed. This was repeated on the twenty-third, the pressure was the same, there was practically no blood in the fluid, and 15 cc was removed. On April 25, 35 cc of bloody spinal fluid was removed. At this time, the pressure was not taken. On the twenty-seventh, the pressure of the fluid was 12 mm of mercury, 25 cc of fluid was removed, and the pressure was thus lowered to 6 mm of mercury.

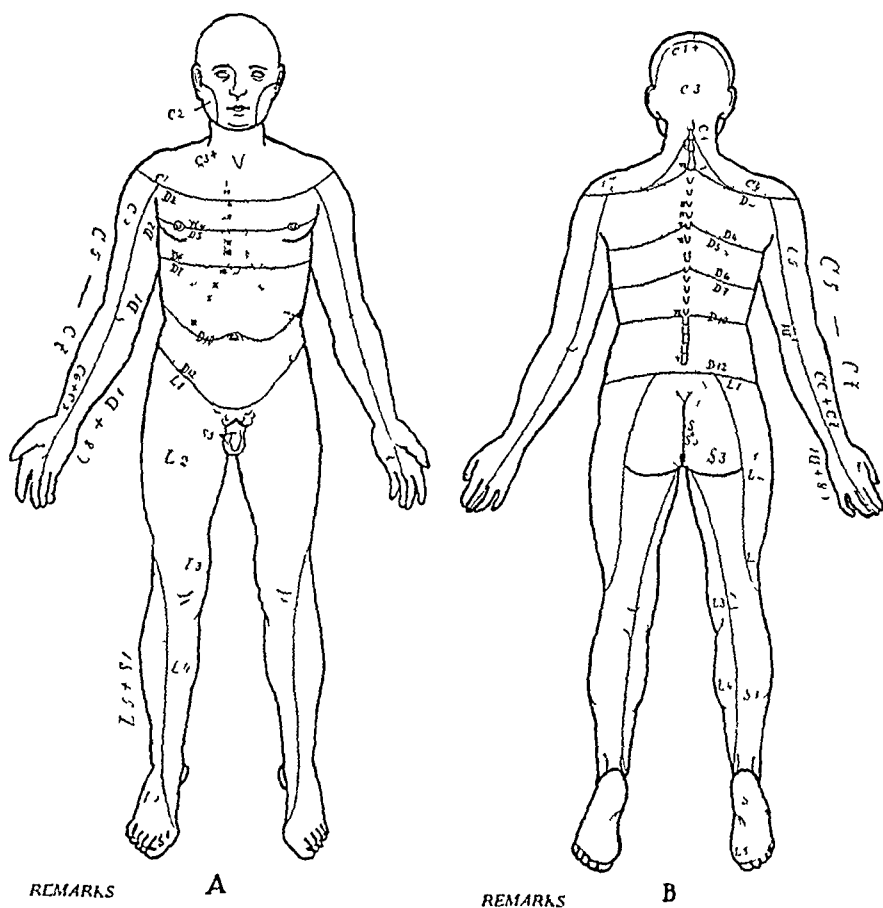


Fig 7—A, chart (anterior view) showing sensory involvement (pain and temperature), B, chart (posterior view) showing sensory involvement (pain and temperature)

To this time, the patient remained in fair condition, the wounds on the head healing satisfactorily, and his back remaining in good condition. On April 28, he had a chill followed by a rise of temperature to 103.6 F. The urine was decreased in quantity, was cloudy, and on examination was found to contain blood and albumin and to be loaded with leukocytes and bacteria. Spinal puncture the following day revealed a pressure of 10 mm of mercury, 25 cc of fluid was removed, and the pressure fell to 6 mm of mercury.

The condition of the patient steadily grew worse, and he died on May 2, seventeen days after his injury.

*Dr Hassin's Observations*—Dr Hassin in a neurologic examination of the patient on April 17 made observations as follows: absence of deformities of the

vertebral column including the cervical region a beginning bed sore in the left gluteal region, normal mentality, normal cranial nerves including those that control the size of the palpebral fissures and the pupils (absence of Horner's syndrome), normal amplitude and force in active and passive movements of the neck, absence of pain and no rigidity in neck, paralysis of the hands and fingers, including the thumbs, inability to flex or extend the wrists and fingers and to abduct the thumbs, absence of spasticity, complete flaccid paralysis of the lower extremities with loss of tendon and plantar reflexes, absence of Babinski's sign, loss of pain and temperature sensibilities up to the level of the fourth thoracic spinal segment, sensory disturbances involving the ulnar surfaces of the forearms and the hands except the thumbs on both sides, preservation of the tactile sense in the areas affected by the loss of pain and temperature sensations, preservation of the position sense, distention of the bladder, with the abdominal walls rigid, spinal fluid slightly tinged with blood

These observations were summarized as "flaccid paraplegia due to a spinal cord lesion at the level of the first or second thoracic segment. The lesion of the spinal cord is not due to a fractured or dislocated vertebra, but most likely to an intraspinal hemorrhage."

The diagnosis was hematovelvia in the cervicodorsal region.

Dr. Hassin's recommendations as to treatment were "Surgical interference not indicated, for there is no evidence of pressure symptoms, prevention of bed sore formation and genitourinary complications, spinal punctures every other day."

*Gross Pathologic Observations*—A postmortem examination of the spinal cord was made by Dr. F. W. Merritt twenty minutes after the patient's death. On making an incision over the spines of the vertebrae, he noted that the space between the spinous processes of the third and fourth thoracic vertebrae was enlarged and that there was no tissue between the two spinous processes so that a finger could be put between them. The spinous processes and laminae from the fourth cervical vertebra to the eighth thoracic vertebra were removed. There was no pressure on the spinal cord by the vertebral column and there were no extradural blood clots.

When the dura and arachnoid were opened, the spinal fluid was found to be clear. There were no subdural blood clots or other evidence of subdural hemorrhage. On the dorsal surface of the cord in the region of the sixth cervical vertebra, the blood vessels appeared to be congested. The spinal cord with its membranes from the fifth cervical to the ninth thoracic segments, inclusive, was removed and placed in a diluted solution of formaldehyde U. S. P. (1:10) for further study.

Later gross examination by us showed the dura around the sixth cervical segment to be discolored, apparently owing to extravasated blood from ruptured blood vessels of the dura itself. When the cord was sectioned transversely in the region of the sixth cervical segment and the cut surface examined with the naked eye, the gray matter on the left side was seen to be definitely outlined by the hemorrhages that had occurred. On the right side, the hemorrhage was not so extensive but was rather of the petechial type. In addition, there were minute petechial hemorrhages in the dorsal funiculus and in the lateral funiculus of the white matter.

*Microscopic Pathologic Observations*—Most of this work was done by the junior author (H. C. V.) in the Hull Biological Laboratories of the University of Chicago during the spring of 1926. The material was prepared for microscopic study by several different methods.



Busch's (1899)<sup>1</sup> modification of the Marchi method for formaldehyde-fixed material was used on blocks taken from the fifth, sixth, seventh and eighth cervical segments and from the first, third, fifth, eighth and ninth thoracic segments. These blocks were placed for from five to ten days (the longer time being preferable) in a mixture of 1 Gm of osmic acid, 3 Gm of sodium iodate and 300 cc of distilled water. The blocks were then washed, dehydrated, imbedded in paraffin and cut into sections from 10 to 15 microns thick. These sections were mounted in the usual way.

Since we felt the need of being able to study the histologic changes in the ventral horn cells in the same material which had been prepared for the study of degenerative changes in the fiber tracts, a method was devised for counterstaining the material prepared by the modification of the Marchi method described. After the paraffin section from this material had been mounted in the usual way, the paraffin was dissolved with xylene, and the sections were run to water. They were then treated with 1 per cent potassium permanganate for one minute and 5 per cent oxalic acid until white and were then counterstained with a 1 per cent solution of neutral red that had been ripened by Morgan's (1926)<sup>2</sup> method. The slides carrying the section were covered with the neutral red solution from a pipet and then were heated until the solution had steamed for from two to three minutes. Then the sections were washed, dehydrated and mounted in the usual way. Used in this way, neutral red is a specific stain for the Nissl substance of the nerve cells. The sections present a pleasing appearance, as the neutral red contrasts well with the black or brown stain of the osmic acid. Sections from the fifth and sixth cervical and from the fifth thoracic segments were prepared by this method.

Blocks from the sixth and seventh cervical and from the ninth thoracic segments were dehydrated and imbedded in celloidin. Sections from 20 to 30 microns thick were cut from these blocks and stained by the standard Pal-Weigert technic.

In addition, blocks from the sixth and eighth cervical and from the second, fifth and ninth thoracic segments were dehydrated and embedded in paraffin. Sections 10 microns thick were cut from these blocks and stained with Delaney's (1927)<sup>3</sup> modification of the Nissl technic. And finally, sections from the sixth cervical and from the second and fifth thoracic segments were stained with hematoxylin and eosin, Erlich's aqueous hematoxylin and alcoholic eosin being used.

As this specimen came from one who had died seventeen days after a lesion to the cord had occurred, degeneration of the myelin sheaths of the myelinated fibers of the cord would be going on, but would not be completed, in this short a time. Hence one would expect material prepared by a technic, such as the Pal-Weigert<sup>4</sup> technic for staining myelin sheaths to fail to show any profound pathologic changes, but material prepared by the Marchi technic for the demonstration of myelin sheaths in the process of degeneration, to show definite pathologic changes. Our material showed these assumptions to be correct.

Casual examination of the Pal-Weigert material disclosed an appearance of normally staining white matter and myelin sheaths, but more careful study with

1 Busch. *Ztschr f wissenschaft Mikr*, 1899, vol 15

2 Morgan L O. Iron Hemotoxylin as a Myelin Sheath Stain and Neutral Red Ripened by Colon Bacillus as a Nerve Cell Stain, *Anat Rec* **32** 283, 1926

3 Delaney, P A. Reliable Methods for the Fixation and Staining of Nissl Substance, *Anat Rec* **36** 111 1927

4 Hardesty, I. *Neurological Technique* Chicago, University of Chicago Press 1902

the high power objective showed that the myelin sheaths of the lateral funiculus in the region of the corticospinal and the rubrospinal tracts were somewhat fragmented and in some cases partly destroyed, presenting a quite different appearance from the normal myelin sheaths of the normal spinocerebellar tracts at the periphery of the lateral funiculus. This condition of partial degeneration of the myelin sheaths obtained more on the right side than on the left, and was seen in sections from the sixth and seventh cervical segments. Sections from the ninth thoracic segment presented a normal appearance as far as could be seen. In other respects, the Pal-Weigert material presented a normal appearance.

The Marchi material from the fifth cervical segment showed a generalized degeneration of the myelin sheaths in the fasciculus cuneatus (B N A) of the dorsal funiculus, in the corticospinal and rubrospinal paths of the lateral funiculus,



Fig 8—Photomicrograph of section of seventh cervical segment (Marchi stain), showing degeneration of the descending fiber tracts,  $\times 135$

and in the ventral funiculus. In the sixth cervical segment, the degeneration in the dorsal funiculus was mainly in the lower part of the fasciculus cuneatus and apparently in the comma-tract of Schultze. In the lateral funiculus, the degeneration of the descending paths was more marked on the right side than on the left, and there was no degeneration at all in Flechsig's bundle or in Gower's fasciculus. There was extensive degeneration in the ventral funiculus, especially in that part bordering on the ventral horn of the gray matter. The same conditions were seen in the sections from the seventh and eighth cervical segments (fig 8).

This general picture changed little throughout the thoracic region except in detail. The degenerated fibers, all belonging to descending paths, became fewer in number as examination went lower in the thoracic region. Thus in the eighth and ninth thoracic segments (fig 9) there were few degenerated fibers in the



Fig 9—Photomicrograph of a section from the eighth thoracic segment (Marchi stain), showing degeneration of the descending fiber tracts,  $\times 135$



Fig 10—Photomicrograph of section through Clarke's nucleus at the fifth thoracic segment, showing chromatolysis,  $\times 300$

dorsal funiculus and those that were present were close to the medial surface of the dorsal horn of the gray matter. In the lateral funiculus the degeneration in the corticospinal and rubrospinal paths was much more abundant on the right side than on the left. And in the ventral funiculus the degenerated fibers were scattered mainly along the ventral median fissure and at the anterior periphery of the ventral funiculus of the cord.

In all the sections treated by the Marchi method black or brown staining droplets could be seen in cells of the gray matter of the ventral horn. These droplets were apparently made up of lipoid materials that took the osmic acid stain and were normally present in the cells of the central nervous system. In the sections from the sixth and seventh cervical and from the fifth thoracic segments that were prepared by the Marchi method and then counterstained with neutral red a few of the cells of the ventral horn showed some degenerative changes in the Nissl substance, but the changes were not marked and there were comparatively few cells showing these changes. However, in the sections from the fifth thoracic segment, the cells of the nucleus dorsalis of Clarke of both sides showed definite chromatolytic changes in the Nissl granules (fig. 10).

The same was true of the sections from the sixth and eighth cervical segments and from the second, fifth and ninth thoracic segments that were stained by Delaney's modification of the Nissl method. There were no marked degenerative changes in the ventral horn cells but in the thoracic region the nucleus dorsalis of Clarke of both sides showed profound chromatolytic changes in its cells. The cells were swollen, the Nissl granules were disintegrated, and the pale nuclei were placed eccentrically in the cells.

#### COMMENT AND SUMMARY

In summary we may say that a portion of the cord taken from the region of the lesion and below and including the last four cervical and the first nine thoracic segments showed degeneration of the descending tracts particularly those of the lateral and ventral funiculus below the site of the lesion. There was a preponderance of degeneration on the right side. In the thoracic region there were degenerative changes in the nucleus dorsalis of Clarke. This latter was indirect evidence that there was a lesion of the fibers of at least one ascending tract, the dorsal spinocerebellar.

The extensive degeneration of descending fiber tracts below the lesion and probably of ascending fiber tracts above the lesion point to a crushing lesion of the cord. The sensory disturbances could readily be explained as the result of a hematoma or particularly of a hemorrhage into the gray matter as the disassociation of pain and temperature sensations from tactile sensation points to that type of lesion. However we feel that such extensive degeneration in the white matter while probably due in part to the hemorrhages noted could not be due to them entirely. The disturbance of the blood supply of the white matter through a distance of two or three segments at the most would not be a sufficient injury of the fibers to cause their degeneration and certainly the hemorrhage as seen at the postmortem

examination was not great enough to cause a pressure sufficient to cause degeneration of the fiber tracts. Myelinated nerve fibers depend mainly on their cells of origin for nutrition and are comparatively resistant to trauma.

#### CONCLUSION

From the consideration of the x-ray pictures, the clinical history, the results of the physical examination and the gross and microscopic pathologic observations, we conclude that this patient sustained an injury of the spinal cord in the nature of a temporary compression of the cord from a fracture dislocation of the sixth cervical vertebra.

The injury here corresponded to the type of buckling injuries in which there is at the time of injury pressure on the spinal cord by a temporary dislocation or fracture dislocation and in which when the causal force is removed, the dislocation is reduced.

# FOCAL INFECTION IN SPONDYLITIS DEFORMANS\*

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Spondylitis deformans is to be differentiated from the deformities of the spine produced by arthritis vertebral tuberculosis, developmental and postural defects, such as scoliosis and round shoulders, and the stiff backs incidental to trauma. As described by von Bechterew, Strumpel and Marie, the spinal disease considered forms a distinct clinical picture with these characteristics: a chronic progressive stiffening of the spine engrafted on a slowly increasing flexion deformity that ultimately leaves the back rigid in a stooped position frequently extending to involve the costovertebral joints to produce a rigid thoracic cage and sometimes involving the hips and shoulder joints. It usually attacks young men in the postadolescent period. The typical case presents a startling picture. The patient walks along with his body stooped far over so that he is facing the ground. To face the person with whom he talks he must rock his entire body back and roll his eyes up. The wall of the chest presents no motion, leaving his respiration entirely abdominal. When lying on his back, his fixed spine retains its semicircular position so that he can be rocked to and fro. The condition is usually distressing not only on account of the pain but also on account of the disability and the deformity. Pathologically, the disease is characterized by an involvement of the perivertebral ligaments, so that as one follows the progress of the condition by roentgen examination one sees an increasing calcification of these ligaments. Autopsies have shown the spinal rigidity to be due to an almost solid layer of bone that surrounds the bodies of the vertebrae.

The treatment for spondylitis deformans has been similar in many ways to that for infectious arthritis of the spine. This would naturally follow the resemblance of the clinical manifestations of this disease in its earlier stages to arthritis of the spine. Furthermore, some authorities feel that the disease is a localized expression of a generalized arthritic process. At any rate, most of the patients suffering with spondylitis have been combed for foci of infection and subjected, when possible to their radical removal.

It has long been felt that in spite of the most careful eradication of such foci, the deforming spondylitis was not being checked. It was to determine the accuracy of this impression that I made a survey of such cases on record at the Johns Hopkins Hospital and of such other cases as have come under my attention. After weeding out those

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\* Submitted for publication April 9, 1929

which did not show the characteristic history and symptoms of spondylitis deformans, I collected sixty-six. Since the handling of the earlier cases differed from that of the later ones, it has been convenient to subdivide them into two groups, those in which the patients were seen before 1916, and those in which they were seen after that date. In the earlier cases, no systematic search for foci was made, but the patients were treated with rest in bed and plaster cast immobilization. In the second group, however, routine treatment consisted of the localization



A patient with spondylitis deformans standing as erect as possible. This patient had previously been stretched with a resultant gain of 5 inches (12.70 cm) in height.

of any infectious process and when possible, the operative correction. In addition to the focal treatment orthopedic measures were applied. Studies of the effect of focal treatment must therefore be based on this second group. This group included fifty-six cases, but in only forty-five of these were foci of infection found: twenty-six occurred in the nose and throat; fifteen in the mouth; and twenty-three in the genito-urinary regions. Gastro-intestinal disturbances were noted in four

patients. Of the twenty-six patients with involvement of the nose and throat, nineteen had had tonsillectomies performed before they sought relief in the clinic. None of these patients reported anything more than temporary relief from symptoms between the period of their operation and their admission to the hospital. In addition to these seven patients had their tonsils removed by members of the staff. Practically all of the patients with infections of the teeth were given the benefits of extraction. The patients with gonorrhea were submitted to massage and irrigation and in two instances, because of delayed response to this therapeutic procedure seminal vesiculectomy and prostatectomy were performed. In two of the patients of the group enlarged lymph glands were removed and cultures were made to produce a vaccine which was used therapeutically.

To justify the recommendation of surgical procedures one should be convinced that at least a fair number of patients are likely to show improvement. The ideal recovery, of course, would constitute a cessation of the disease process followed by the complete functional restoration. Since, however at times there is already considerable fusion of the vertebrae when the patients themselves one would be justified in considering one's efforts rewarded if the disease process could be stopped even though complete mobility of the spine could not be restored. On the other hand since the disease is after a fashion, self-limited that is, runs on to a state of complete spinal rigidity at which time the symptoms of pain clear up, one must be careful not to attribute to the removal of foci of infection the freedom from pain that comes long after the focal treatment has been completed.

With these criteria in mind a survey of the cases fails to show one distinct instance of lasting improvement following the removal of foci of infection. Indications of the failure of this procedure could be noted in the fact that so many of the patients came for treatment in spite of their earlier careful focal treatment. A follow-up of patients on whom focal eradication was performed likewise failed to show improvement. From these observations one is forced to admit the futility of focal treatment in spondylitis deformans.

Much more favorable results followed the orthopedic maneuvers. Working on the assumption that the condition of the spine would in all likelihood progress to a state of rigidity, efforts were directed toward obtaining as good a posture as possible and then holding the improved position till the fusion had taken place. Since most of the patients who presented themselves were already rather bowed an attempt was made to straighten them by having them lie on their backs on a springless bed (fracture bed) or on a Goldthwaite frame. The effects of gravity in straightening the patients thus treated were in many cases striking. One man after resting two hours daily on his back for a



period of two months gained 5 inches (12.70 cm) in height as his curvature was being corrected. In some instances head and pelvic traction was necessary. In all, this process of slow stretching was attended by severe pain, often necessitating the use of opiates during the stretching periods. In none of the patients was forcible manipulation attempted under an anesthetic because of the obvious dangers. I feel that this conservative course is to be credited with the freedom from neurologic accidents shown in the records of these cases.

After the patient had been straightened, or after as much straightening had been obtained as was justified by the stretching process, a plaster of paris support was made. This permitted the patient to become ambulatory and in most instances to return to work, without again developing his deformity. By observing the clinical symptoms and by roentgen studies from time to time, one was able to determine when the disease had run its course. As a rule, this happened when fusion had taken place. At that time the support could be removed without fear of recurrent deformity. The patient was stiff in the erect position, was able to walk upright and could meet the world face to face. It is true that on attempting to stoop and bend from side to side he had to resort to motion at the hips and knees, yet the freedom from pain allowed this to be done without any great discomfort. It is a matter of interest, also, that in those patients in whom ankylosis in the erect position was allowed to occur the complications of the hip and knee were not observed.

The deductions are clearcut. While one cannot gainsay the propriety of removal of gross, obvious foci of infection for general hygienic purposes, I feel justified in concluding from these studies that the results do not warrant radical operative procedure performed with the idea of removing the causative factor of the spondylitis. I particularly wish to stress the importance of close attention to the collective orthopedic procedures which, though only symptomatic, offer the one hope of actual improvement.

# Fortieth Report of Progress in Orthopedic Surgery \*

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## CONGENITAL ABNORMALITIES

*Club Feet*—Boehm<sup>1</sup> carefully studied the normal human embryo foot at two, three and four months and found interesting parallels to the shape of the club foot. For comparison he prepared the club feet of a 7 months old fetus after the method of Hans Virchow, preserving the topographic position of the bones as they were in the original specimen. The comparison showed that the marked right-sided clubfoot had a great similarity to the embryonic foot of the fifth or sixth week and that the lighter left-sided clubfoot was almost a reflected image of the embryonic foot of the twelfth week. Boehm concluded that the congenital clubfoot represented an arrested development.

*Congenital Dislocation of the Hip Joint*—Krida<sup>2</sup> in discussing a series of thirty-one cases released from fixation dressings in children of an age group up to 3 years said that twenty-eight might be considered to be satisfactory results in periods of observation up to two years. Minor deviations from anatomically normal hips would have to be evaluated at a much later time.

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\* Submitted for publication Dec 10 1929

This Report of Progress is based on a review of 313 articles selected from 523 titles dealing with orthopedic surgery appearing in medical literature between Feb 15 and June 1 1929. Only those papers which seem to represent progress have been selected for note and comment.

1 Boehm M. *Ztschr f orthop Chir* **51** 409 1929

2 Krida A. *Am J Surg* **61** 185 (Feb) 1929

His method of procedure in this age group was manual reduction with a minimum trauma. At the first sitting, the hip was fixed in plaster in the original 90-90 degrees attitude of Lorenz, except that the dressing was carried below the knee. This position was maintained for two weeks. At the second sitting, the anterior distortion was evaluated by a study of the roentgenograms made before reduction but particularly of what might be gained by palpation of the structures of the hip joint. The abduction was carefully reduced to about 25 or 30 degrees, and the patella brought into the sagittal plane. If the head remained deeply placed in the tissues of the groin and in its proper relation to the femoral artery, it might be assumed that no abnormal anterior distortion was present. The limb was fixed in this position until the end of treatment. If the head became prominent in the groin and if on even slight outward rotation of the extremity it became displaced slightly laterally to the line of the femoral artery, it might be assumed that a degree of anterior distortion existed which was inimical to the ultimate security of the joint. This hip was then put into forced internal rotation and left there for three months.

At a third sitting, by means of manual force a supracondylar fracture was made, and this usually occurred in the segment above the epiphyseal line. Outward rotation of the lower fragment was made until the patella lay outside the sagittal plane. A plaster spica was applied with the lower fragment in this position and in about 20 degrees of abduction and slight flexion of the hip and knee joints. This plaster was worn for two months, thus giving in the ideal case a period of fixation of somewhat less than six months. During the last month of fixation, the patient ought to stand and make attempts at ambulation.

[ED NOTE—This work represents a logical attempt to solve a difficult complication of congenital dislocation of the hip, and it will be interesting to receive further reports of the late results.]

#### THE SPINE

*Anatomic Variations*—In five of fifty-six Bantu skeletons, Shore found an anomalous mode of development of the lower lumbar vertebrae resulting in the separation of the dorsal arch by a congenital cleft. One of the five exhibited a spondylolisthesis. Willis<sup>4</sup> found this congenital division of the vertebral lamina in the skeletons of 31 of 748 Americans (white and colored).

Cushway and Maier recommended that a roentgenologic examination be made of all employees in industries in which injuries of the

3 Shore, L. R. Brit J Surg **16** 431 (Jan) 1929.

4 Willis, I. A. Am J Anat vol 32 p 95.

5 Cushway, B. C. and Maier, R. J. Routine Examination of the Spine for Industrial Employees. J A M A **92** 701 (March 2) 1929.

spine are common. This form of examination would prevent the employment of those unfit for certain types of labor. Just compensation to the injured would be certain as this form of examination would definitely fix the date of injury within the term of employment.

Cushway and Maier had made this examination as a routine measure in all the regular examinations of employees and had found that anomalies were common and did not necessarily cause painful backs. There was a total of 931 cases, and 607 variations were found in 414 cases. The total number of congenital and developmental anomalies was 510. The types of observations were: spina bifida occulta, 161; scoliosis, 81; lumbar ribs, 81; proliferative changes, 63; sacralization, 50; deformity of the coccyx, 32; six lumbar vertebrae, 25; incomplete union of the first and second sacral segments, 21; and deformity of the transverse processes, 14.

Bohart<sup>6</sup> wrote that a study of practically 1,000 symptomless spines showed approximately 44 per cent of anomalies and anatomic variations. Spina bifida occulta was noted most commonly, and sacralized transverse processes came next in frequency. With the exception of the spines which showed tipping or spur formation there did not seem to be any lengthened disability or any increased tendency to injury over the normal spine.

[ED. NOTE—These figures give a fairly accurate estimate of the relative importance of congenital anomalies.]

*Pathologic Lesions of the Spine*—Experiments on the cadaver made by Chassin<sup>7</sup> showed that destructive changes in the vertebrae had to be of considerable size to be noted on the roentgenogram. A defect of from 1 to 1.5 cm. width could not be seen. Defects of one fourth of the body were not seen provided the cortical layer was intact, and in the sacral vertebrae complete defect of the spongy layer was not visible if the cortex was preserved. Schmorl<sup>8</sup> from his unusual experience in the study of the pathology of the vertebrae described certain peculiarities of infantile and adult vertebrae heretofore not sufficiently known. On the upper and lower surface of the body after removal of the intervertebral disk a sieve-like perforated plate was noticed surrounded by a border without holes. The holes undoubtedly served the nutrition of the disk. On the other hand, the juvenile vertebra showed on the upper and lower surface small radiating furrows and irregularities. In Schmorl's opinion, the so-called epiphysis of the body of the vertebra was not a structure of comparable value to the epiphyses

6 Bohart W. H. Anatomic Variations and Anomalies of the Spine. J. A. M. A. **92**: 698 (March 2) 1929.

7 Chassin A. Fortschr. u. Geb. d. Röntgenstrahlen 1929, vol. 37, no. 4.

8 Schmorl G. Arch. f. klin. Chir. **150**: 420 1928.

of the long bones and had nothing to do with the growth of the vertebrae. With advancing age, Lyon<sup>9</sup> noted that the intervertebral disk was the most frequently and most early affected part of the spine. Presenile aging, infectious diseases and other diseases played the primary rôle. The anatomic changes consisted of fibrillation, softening decay and fatty degeneration, frequently followed by calcification, i. e., processes resembling those of arteriosclerosis. These changes of the intervertebral disks were followed by the well known changes at the borders of the vertebral bodies which were not primary but secondary.

[ED. NOTE.—This observation is true and follows the course outlined by Nichols and Richardson for degenerative arthritis in other joints.]

#### THE FOOT

*The Normal Foot*—Among other interesting statements made by Sir Arthur Keith<sup>10</sup> in the third Hugh Owen Thomas lecture in which he traced the history of the human foot was the observation that man's mode of progression resulted in an increase in the supporting or tarsal elements and a lessening of the digital or prehensile parts of the foot. Sir Arthur traced in detail the changes which transformed the prehensile foot of the ape into the static foot of man, taking up the evolution of the plantar fascia and of the various muscles. He pointed out that as the hallucal element of the foot became incorporated in the plantar arch it was done by adduction not of the great toe to the outer toes but of the outer toes to the great toe. He further emphasized that the primary factors in maintaining the balance of the foot were the muscles and not the bones or ligaments.

#### NUTRITIONAL AND METABOLIC DISTURBANCES OF BONE

*Rickets*—Tisdall and Brown,<sup>11</sup> in an interesting study of the relation of the altitude of the sun to its antirachitic effect, stated: 1. A marked increase occurred in the antirachitic effect of sunshine when the sun reached an altitude of 35 degrees or more. 2. A study of the geographic distribution of rickets showed that rickets was uncommon or existed chiefly in a mild form in those places where the minimum seasonal altitude of the sun was not much less than 35 degrees. 3. Conversely, severe rickets was chiefly encountered in those cities where the altitude of the sun was below 35 degrees for some months of the year. 4. The period of the year during which rickets would probably develop could be calculated for any city in the world. The duration of this period

<sup>9</sup> Lyon E. *Arch f orthop Chir* **26** 295, 1928.

<sup>10</sup> Keith Arthur. *J Bone & Joint Surg* **11** 10 (Jan.) 1929.

<sup>11</sup> Tisdall F. F. and Brown A. Relation of the Altitude of the Sun to Its Antirachitic Effect. *J A M A* **92** 860 (March 16) 1929.

might be altered however, by the prevention of exposure of patients to highly effective sunshine on account of inclement spring weather or other factors

*Parathyroids*—During recent years the excision of one or more parathyroid glands has been performed in cases of generalized osteitis fibrosa. Mandl<sup>12</sup> pointed out the danger of the uncritical removal of the parathyroids. If a tumor of one is found the others should be examined surgically, and, if normal, the tumor may be removed. If all the parathyroids are enlarged, frozen sections should be examined to determine whether enough normal parathyroid substance is present before one or more is excised.

#### TUMORS

Putti<sup>13</sup> agreed with John B. Murphy "that in cases of sarcoma the diagnosis could and should be made entirely by the history and with the aid of skiagrams." He said that trauma was of the greatest importance. Isolated direct trauma was likely to induce a tumor of the peripheral layers with a short latent period whereas indirect trauma, distortions and fractures were more likely to be causes of sarcomas with a long latent period and a central situation. The author believed that there were few pathologists who possessed the art of making a differentiation of pathologic conditions in the light of the best interest of the patients. Putti preferred the classification of Nove-Jusserand and Tavernier and the more schematic one of Ewing. Phemister<sup>14</sup> classified the types of tumor of the bone, both benign and malignant and discussed their diagnosis from the roentgenologist's standpoint. He felt that most sarcomas of the bone had metastasized before they were recognized. Consequently, one ought to learn to recognize benign lesions and treat them promptly by appropriate operative measures. Amputation for benign tumors was rarely indicated and roentgen treatment was of no value.

[ED. NOTE—In spite of the efforts of some, the whole question of tumors of the bone seems very much of an enigma to the average man. Certainly the pathologists who see these cases can help and one must depend on them a great deal in deciding the treatment.]

#### TUBERCULOSIS

Cleveland and Pyle<sup>15</sup> reported the cases of sixty patients with tuberculosis of the bone and joint treated by operation, with 53.3 per cent good results and twelve deaths. They argued from the standpoint of

12 Mandl F. *Zentralbl f Chir* 56 1739 1929

13 Putti V. *Surg Gynec Obst* 48 324 (March) 1929

14 Phemister D. B. *Northwest Med* 28 1 (Jan) 1929

15 Cleveland M. and Pyle F. *Joint Tuberculosis* J. A. M. A 91 1406 (May 4) 1929

economy that operative treatment brought about a saving in costs to the patient and to the community

[ED NOTE—This may well be true but their end-results do not show a high percentage of good results. After all, these are more important than costs. The costs may be dependent too on the type of conservative treatment received.]

Doub and Menagh<sup>16</sup> reported the cases of two patients showing indolent, painless, nonulcerating granulomas of the subcutaneous tissue or sarcoid of the Beck and Darier-Rousay type associated with slowly progressive alteration of the trabecular formation of the bones followed by actual destruction as the lesion progressed. The phalanges were most frequently involved, although the metacarpals and metatarsals also showed lesions. One case showed involvement of the lower end of the radius. While the etiology was not indisputable, most of the evidence, both clinical and experimental, pointed to the tubercle bacillus as the etiologic factor.

By repeated routine inoculations of urine into guinea-pigs Harris<sup>17</sup> showed that tubercle bacilli were present in the urine in 37 per cent of adult and 14 per cent of children suffering from tuberculosis of the bone or joint. Although this bacilluria was unaccompanied by symptoms of renal tuberculosis, Harris adduced evidence to show that it signified a tuberculous lesion of the kidney and not simply the excretion of the tubercle bacilli by the kidney from the blood stream.

With improved antigens prepared from human and bovine tubercle bacilli, Thjøtta and Gundersen<sup>18</sup> carried out complement-fixation tests in 325 specimens of blood serum. The authors felt that the test could not be compared with the Wassermann test in syphilis. Its value was not great in pulmonary tuberculosis, and no dependence could be placed on it in tuberculosis of the bones and joints or in tuberculosis of the skin.

#### PYOGENIC AND OTHER INJECTIONS

Wilensky<sup>19</sup> found the spine involved in only 9 of 578 cases of osteomyelitis, 1.5 per cent. The mortality rate was high from 35 to 45 per cent. Cases in which the posterior neural arch was affected gave the best prognosis.

Porter and Rucker<sup>20</sup> treated five patients with acute gonococcal synovitis of the knee joint with serofibrinous or purulent exudates with aspiration and air insufflation. They said that the relief from local and

16 Doub H P and Menagh F R. *Am J Roentgenol* **21** 149 (Feb) 1929.

17 Harris R I. *Brit J Surg* **16** 464 (Jan) 1929.

18 Thjøtta T and Gundersen F. *Am Rev Tuberc* **19** 212 (Feb) 1929.

19 Wilensky A O. *Ann Surg* **89** 561 (April) 1929.

20 Porter W B and Rucker J E. *Air Insufflation in Treatment of Acute Gonococcal Synovitis of Knee Joint*, *J A M A* **92** 1513 (May 4) 1929.

constitutional symptoms had been prompt and lasting. In no case had there been an aftermath of partial ankylosis. A return to normal function had occurred within an average of twenty-three days.

#### ARTHRITIS

Bervl Harding<sup>21</sup> demonstrated that muscles that wasted as a sequel to arthritis showed a great increase in oxygen consumption (8.3 cc compared with the normal 4.6 cc per one gram of muscle per one minute) whereas muscles that wasted as a sequel to disuse showed a normal consumption of oxygen (5.1 cc). She suggested that this increase was the result of an increased catabolism and that atrophy resulted from the failure of the reparative powers to keep pace with the undue tissue breakdown. In disuse atrophy there was no increased catabolism but simply an impairment of the synthetic powers of the affected muscles. Harding postulated that the increased catabolism might be due to an increase in the number of sensory impulses arising in the joint and in proof of this she found that division of the posterior nerve roots supplying the arthritic joint prevented the muscle from wasting. The experiments were controlled.

[ED NOTE—This seems to us a really important contribution to the knowledge of atrophy. The facts seem to show that there is more than a simple disuse atrophy in certain of these cases.]

Pemberton<sup>22</sup> in discussing the rationale of physiotherapy in arthritis, noted that the only undoubted influence of massage, heat and exercises was through their effect on the peripheral circulation. Exercise induced a systematic acidosis that led to alkalosis while massage had no such influence on the acid base equilibrium.

Haden<sup>23</sup> believed that practically all cases of acute arthritis were due to infection. In chronic atrophic arthritis all evident foci of infection ought to be removed usually in teeth, tonsils and sinuses. It should be remembered that arthritis represents the interaction of focus and patient. He said that many chronic infections occurred without arthritis. Much more could be expected clinically from the removal of an active infection than from the elimination of a mild symptomless one. Chronic hypertrophic arthritis was not primarily an infectious disease. Foci of infection should be removed because they were harmful in themselves not because their removal might influence the disease.

[ED NOTE—Neither of these articles presents anything particularly new on the subject. Haden's stand on infection is apparently growing stronger. His point as to active infections is perhaps true but to decide as to the activity of such an infection is a difficult matter.]

21 Harding A E B. *Lancet* **1** 433 (March 2) 1929.

22 Pemberton R. *Radiology* **12** 235 (March) 1929.

23 Haden R L. *J Missouri M A* **26** 1 (Jan) 1929.



## DISORDERS OF THE NERVOUS SYSTEM

Steindler,<sup>24</sup> in a preliminary report, attempted by using the oscillograph to determine the effect of sectioning the ram communication of the sympathetic system. He reviewed briefly the anatomic, physiologic and clinical evidence for the rationale of this procedure, the importance of which was emphasized by Hunter and Royle a few years ago. Using the gastrocnemius and the quadriceps muscles, he recorded the four stages of muscular action (rest, beginning innervation, maximum innervation and relaxation) in normal persons, in a patient with Buerger's disease following sympathetic ramisection, in another patient with hemiplegia and in a case of muscular dystrophy. In the last three there was a distinct reduction in the rate of oscillation of the action current. Following ramisection in a case of spastic paralysis, there was also reduction in the frequency and amplitude of oscillations on the sympathectomized side. These observations suggested to Steindler that following ramisection there was considerable change in the response of the sympathetic system, but whether it was due entirely to the elimination of the innervation or secondarily to changed metabolism (altered blood supply as suggested by Cobb) could not be determined.

Pollock and Davis,<sup>25</sup> after experiments with decerebrate animals, were of the belief that there was a wholly new mechanism to explain the plasticity and the lengthening and shortening reaction of muscles. It was not in harmony with the all-or-none activity of individual fibers, which was the basis of the Sherrington conception. They said that the extensibility of a muscle during a tonic reflex might be an intermediate state of muscle contraction. The opposing muscle was dependent on the integrity of the posterior roots for the property of shortening to accommodate to the lengthening of the agonist with a proved adjustment to new length and load against which it works.

Wilfred Harris<sup>26</sup> recorded two instances of pressure neuritis of the deep branch of the ulnar nerve, in a bootmaker and a motor cyclist, respectively. The paralysis was limited to the abductors and adductors of the three outer fingers and the adductors of the thumb. There was no wasting of either thenar or hypothenar eminence, and no weakness of abduction or opposition of thumb and little finger. Great difficulty was experienced in writing and in picking up a pin. Harris could find no reference to this occupational pressure neuritis in the literature but Wooster-Drought<sup>27</sup> fourteen days later wrote that he had seen four similar cases in the past two years.

24 Steindler A, and Lindemann, E. *J Bone & Joint Surg* **11** 1 (Jan) 1929

25 Pollock L J, and Davis, L. Muscle Tone Extensibility of Muscles in Decerebrate Rigidity, *Arch Neurol & Psychiat* **21** 19 (Jan) 1929

26 Harris Wilfred. *Brit M J* **1** 98 (Jan 19) 1929

27 Wooster-Drought, C. *Brit M J* **1** 247 (Feb 9) 1929

## MISCELLANEOUS

*Some Aspects of the Physiology of Muscular Exercise*—By studies of cardiac output, pulse rate, blood flow, vital capacity of the lungs and chemical changes in the blood, Bock<sup>28</sup> and his co-workers were able to show that vast differences existed between athletes in training and persons of sedentary existences in their reaction to muscular exercise. DeMar, the famous Marathon runner, was compared to three persons leading much less active lives. The studies demonstrated that systematic physical training carried out over long periods of time increases the lung capacity, induces a slow pulse rate, increases the stroke volume of the heart, reduces systemic blood pressure during work and apparently greatly increases the oxidation capacity of the muscle cells.

[ED. NOTE—Bock's studies are of great clinical importance in that by estimating these various factors accurate knowledge can be obtained concerning a patient's physical fitness. The neurasthenic person, for instance, although apparently unable to perform many tasks may be found by these studies actually to be capable of rather strenuous exercise. On the other hand, a person convalescing from a prolonged illness will show low reserve power.]

*Painful Shoulder*—Perkins<sup>29</sup> separated four clinical types from the many examples of painful shoulder: (1) Adhesions around the joint characterized by limitation of movement at the shoulder joint through the outer half of its range. It is curable by manipulative surgical intervention. (2) The so-called subdeltoid bursitis which he preferred to call tendinitis, characterized by painful movements through a small arc in the middle of the normal range. It is curable in the hyperacute stage by operation (removal of the calcareous nodule in the tendon of the supraspinatus) and in the acute stage by resting the shoulder joint in partial abduction, with the assistance of time. (3) Osteo-arthritis of the shoulder joint, characterized by painful extremes of movement. It is incurable but capable of alleviation by physiotherapy. (4) Subacute arthritis of the shoulder joint characterized by muscle spasm at the commencement of movement. The patient should be treated by rest on an abduction splint and the eradication of septic foci from the body.

Brailsford<sup>30</sup> examined roentgenographically 347 patients complaining of pain in the region of the shoulder. Fifty per cent showed no abnormality. The commonest change to be noted was osteo-arthritis of the acromioclavicular joint (7 per cent) and osteo-arthritis of the shoulder joint (3 per cent) shown by pointing and irregularity of the articular margins. Undetected fractures were present in 3 per cent.

28. Bock, A. N. *New England J. Med.* **200**: 638 (March 28) 1929.

29. Perkins, G. *Proc. Roy. Soc. Med. (Sect. Orthop.)* **22**: 20 (Feb.) 1929.

30. Brailsford, J. F. *Brit. M. J.* **1**: 290 (Feb. 16) 1929.

and loose bodies in 1.5 per cent. Tuberculosis accounted for 4 per cent. Brailsford believed that the areas in the head of the humerus, described by A. L. Fisher<sup>31</sup> as due to focal necrosis brought about by amebic infestation, are varieties of the normal cancellous structure of the head of the humerus.

[ED. NOTE.—Perkins' classification of the causes of shoulder pain is simple and of practical value. Injury of the supraspinatus tendon should be included as another cause of pain. Codman's studies have shown this condition to be much more common than is supposed.]

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<sup>31</sup> Fisher, A. L. J Bone & Joint Surg **10** 46 (Jan.) 1928

*(To be Concluded)*

# Correspondence

## "CARCINOMA OF THE MALE BREAST"

*To the Editor* —In April, 1927, I published an article in the ARCHIVES under the title given. It contained a table showing data on the cases of forty-one patients who were alive at that time.

### *Follow-Up Data on the Forty-One Patients*

Operator	Case Designation	Date of Operation	
Hodge	W F M	3/28/11	Well 10/23/20
Hubbard	M N	10/ 4/13	
Mackenzie	N	5/ 3/15	Well July 1929
Berg	J G	8/ 7/17	
Deaver	J F	5/24/19	Died 3/9/25 apoplexy said to be free from cancer
Judd	No 5	7/ 7/19	Well 11/7/28
Berg	H	5/20/20	Well June 1929
Lee	J O N	9/17/20	Died 8/19/27 recurrence
Colvin		1/19/21	Well 11/18/28
Wood	J O C	1/25/21	Well 10/17/28
Buchanan	J C	6/22/21	9/5/29 cancer free health poor
Adair	S A A	9/22 21	Well June 1929
Coley	C B	7/ 7/21	Died recurrence Feb 15 1929
Cheever		2/ 4/22	Died December 1927 apoplexy said to be cancer free
Holman	J L	3/ 3/22	Well August 1927
Moschowitz	S	6/17/22	Well 6/20/29
Judd	No 17	1922	Died six years later following an operation nature unknown
Whipple	W M	1/21/23	Well 6/29/28
Lee	G D E	2/ 3/23	Well 6/20/29
Bloodgood	J A J	2/23/23	Died 1/9/29 recurrence
Berg	C D	3/29/23	Well June 1929
Berg	S P	5/ 1/23	Well June 1929
Sumner	M K	7/17/23	Well October 1928
Capwell	F Q	7/ 7/23	Died 4/7/28 recurrence
Cooke	A W J	2/ 9/24	Well Nov 5 1929
Auchincloss	W P	2/20/24	Well October 1928
Cameron		5/13/24	Died October 1926
Jeanneney	No 1	3/29/24	Well 11/30/28
St John	F W	7/ 2/24	Well 2/7/29
Old	R W S	8/23/24	Well 6/21/29
Woolf	G W	7/31/24	October 1927 alive with recurrence in chest and abdomen must be dead now 7/23/29 could not get further data
Speed	M C	9/ 9/24	Died 11/2/27 recurrence
Judd	No 7	12/24/15	Died August 1917 recurrence
Adair	M R	2/ 7/25	Returned to Italy to live and cannot be found
Boughton	J A S	5/26/25	Well June 1929
Sullivan	J H G	8/29/25	Well October, 1928
Tannenbaum	F A	9/ 5/25	Well 7/1/29
Peck	C McK	9/15/25	Well June 18 1929
Judd	No 14	1925?	Died one year five months after operation said to be from influenza and free from cancer
Morgans	E M	6/ 1/26	
Propst	M B	6/18/26	Well August 1929

This list has been followed up as well as possible, and the data so far as available at the present date are set forth in the accompanying table.

Of the forty-one, no later record could be obtained from four. Eleven have since died, mostly of recurrence at the following periods after operation: eight years and ten months, six years and eleven months, eight years, five years and

ten months, six years, five years and eight months, four years and nine months, two years and five months, three years and two months, one year and eight months, and one period unknown

Twenty-six are known to be alive at various periods, the longest being eighteen years and five months. Seventeen are alive more than five years after operation. The latter figures are important as previous to this study it was considered by some writers that no male patient with a proved case of carcinoma of the breast had lived for five years after operation.

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## PHRENICECTOMY IN THE TREATMENT OF PULMONARY DISEASES

AN ANALYSIS OF SIXTY-THREE CASES \*

JULIAN A. MOORE, M.D.

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While much has been written about phrenicectomy, few reporters have evaluated the results of the operation in a large series of cases. This article, in which the late results of phrenicectomy performed by the surgical staff of the University Hospital for various pulmonary diseases are considered, is presented as a contribution toward a better appreciation of the indications for the procedure.

### HISTORY

In 1911, Stuertz<sup>1</sup> first suggested paralyzing half the diaphragm by division of the phrenic nerve in the base of the neck, in order to relax a diseased lower lobe which could not be compressed by artificial pneumothorax. He believed that it was especially indicated in basal bronchiectasis and tuberculosis. Sauerbruch,<sup>2</sup> in 1913, reported five cases in which he had performed phrenicotomy.

In the next few years the operation was performed by other European surgeons for a variety of pulmonary lesions. Walther,<sup>3</sup> in 1914, showed that simple phrenicotomy did not completely paralyze the diaphragm in more than 50 per cent of cases and that in 20 per cent of the cases normal function returned.

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\* From the Department of Surgery, University Hospital, the University of Michigan Medical School.

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1 Stuertz. Künstliche Zwerchfelllähmung bei schweren chronischen einseitigen Lungenerkrankungen. *Deutsche med. Wchnschr.* 37:2224, 1911.

2 Sauerbruch, F. Die Beeinflussung von Lungenerkrankungen durch künstliche Lähmung des Zwerchfelles (Phrenikotomie). *München med. Wchnschr.* 60:625, 1913.

3 Walther, H. E. Röntgenologische Untersuchungen über die Wirkung der Phrenikotomie. *Beitr. z. klin. Chir.* 90:358, 1914.

Goetze<sup>4</sup> and Felix<sup>5</sup> showed that from 20 to 80 per cent of persons have one or more accessory phrenic nerves and that the suprapleural sympathetic plexus sends motor fibers to the diaphragm through the phrenic nerve. In order to insure complete paralysis of half of the diaphragm, Goetze<sup>4</sup> proposed his radical phrenicectomy in which he exposed the phrenic nerve, freed it from connecting sympathetic fibers, resected 1 cm or more, exposed the nerve to the subclavius, which nearly always contains the accessory phrenic fibers when present, and resected 2 cm of it. Felix<sup>6</sup> proposed evulsion or excision of the nerve for a distance that would insure breaking its connection with the suprapleural plexus and all accessory nerves.

The work of Felix and Goetze served to popularize the operation on the continent. The excellent monograph of John Alexander,<sup>7</sup> "The Surgery of Pulmonary Tuberculosis," popularized the operation in America.

#### ANATOMIC AND PHYSIOLOGIC EFFECTS OF PHRENICECTOMY

Interruption of the phrenic and accessory phrenic nerves causes an immediate paralysis and subsequent atrophy of the corresponding half of the diaphragm, which remains in the position of expiration and rises still higher as atrophy progresses. It may rise from 1 to 10 cm on the right and from 1 to 8 on the left side, the maximum rise often occurring weeks or months later. During normal inspiration it may descend slightly because of the tug exerted directly by the unparalyzed side. In forced respiration or on sniffing, the paralyzed side moves paradoxically.

After excision or radical phrenicectomy the muscle does not regenerate, although Zadek and Sonnenfeld<sup>8</sup> reported one case of return of normal function eighteen months after excision. In one of our own cases an evulsion of 10 cm of the left phrenic nerve and a resection of 1 cm of the nerve to the subclavius were done. Immediately after operation and two months later there were definite paralysis and paradoxical movement of the left side of the diaphragm as shown by the fluoroscope.

4 Goetze, Otto. Die radicale Phrenikotomie als selbstandiger therapeutischer Eingriff bei der chirurgischen Lungentuberkulose, *Arch f klin Chir* **121** 244, 1922, Die radicale Phrenikotomie als selbstandiger therapeutischer Eingriff bei einseitiger Lungen-phthisis, *Klin Wchnschr* **1** 1496, 1922.

5 Felix, Willy. Anatomische experimentelle und klinisch Untersuchungen uber den Phrenikus und uber die Zwerchfellinnervation, *Deutsche Ztschr f Chir* **171** 283, 1922, Untersuchungen uber den Spannungszustand und die Bewegung der gelahmten Zwerchfelles, *Ztschr f d ges exper med* **33** 458, 1923.

6 Felix (footnote 5, first reference).

7 Alexander, John. *Surgery of Pulmonary Tuberculosis*, Philadelphia, Lea & Febiger, 1925, vol 15, p 175.

8 Zadek, quoted by Sonnenfeld, Arthur. Klinisch Beitrage zum Wirkungs-mechanismus der isolierten Phrenikus-Exstirpation, *Beitr z Klin d Tuberk* **69** 340, 1928.

Nine months later fluoroscopic examination showed paradoxical movement of the left side of the diaphragm on sniffing, but on forced inspiration an excursion of 3 cm of normal motion, the left side of the diaphragm lagging behind the right

The rise of the diaphragm decreases the capacity of the lung from one-fourth to one-third (Gercelez<sup>9</sup>), or from 400 to 800 cc (Brunner<sup>10</sup>). It partially compresses and relaxes the lung and abolishes the tug of the diaphragm on the diseased lung. As a rule the rise of the diaphragm interferes in no way with respiration nor does it produce dyspnea. Lemon<sup>11</sup> has shown this by his experiments on dogs. Dunner, Lasar and Mecklenburg<sup>12</sup> reported the case of a child who had a bilateral phrenico-exeresis done without respiratory difficulty. It usually makes cough and expectoration easier, though sometimes the reverse is true.

#### RATIONALE OF THE PROCEDURE

The therapeutic ideal in the treatment for pulmonary diseases is rest. Surgically, it is best obtained by (1) artificial pneumothorax, (2) thoracoplasty, (3) multiple intercostal neurectomy plus phrenicectomy and (4) phrenicectomy, in the order named. The latter only partially rests and compresses the diseased lung, and because of this incompleteness it cannot take the place of the other three methods. However, the added rest and compression given by paralysis of the hemidiaphragm are often enough to influence markedly the pathologic condition.

Most observers ascribe the beneficial effects of hemidiaphragmatic paralysis to the partial rest, relaxation and compression of the diseased lung thus produced and to the diminution of the amount of toxins pumped into the circulation. Dunner, Lasar and Mecklenburg<sup>13</sup> denied that any compression or rest of the lung occurs and expressed the belief that interference with the vagus and sympathetic fibers to the lung during evulsion of the nerve explains the effect. Sergent and Baumgartner<sup>14</sup> expressed the belief that the effect of phrenicectomy is

9 Gercelez, quoted by Sonnenfeld. *Beitr z Klin d Tuberk* **69** 340, 1928

10 Brunner, A. Die Prognose bei der operationen Behandlung der Lungentuberkulose, *Arch f klin Chir* **121** 482 1922

11 Lemon, W S. The Physiologic Effect of Phrenic Neurectomy. *Arch Surg* **14** 345 (Jan) 1927

12 Dunner, Lasar and Mecklenburg. Max. Zum Wirkungsmechanismus der Phrenikus Exhairese. *Ztschr f Tuberk* **46** 406 1926

13 Dunner and Lasar. Zur Frage der Phrenikus Exhairese. *Ztschr f Tuberk* **49** 31 1926. Dunner and Mecklenburg. Der Einfluss der Phrenikus Exhairese auf die Atmung. *Deutsche med Wchnschr* **52** 1819 (Oct) 1926. Footnote 12

14 Sergent E and Baumgartner R. A propos de huit cas de phrenicectomie. *Bull et mem Soc med d hop de Paris* **42** 20 (Jan) 1926



In group 2 there were five cases of pulmonary tuberculosis in which after phrenicectomy was done to supplement pneumothorax the expectation was fulfilled in 80 per cent. Figure 2 illustrates how phrenicectomy may increase the collapse obtainable by pneumothorax.

The indication in one of the cases was to stop movement of the right side of the diaphragm and to increase the collapse. The condition of the patient improved.

In three cases, phrenicectomy was done to supplement pneumothorax and to increase collapse. In two of the patients the condition improved and in one it was unimproved.

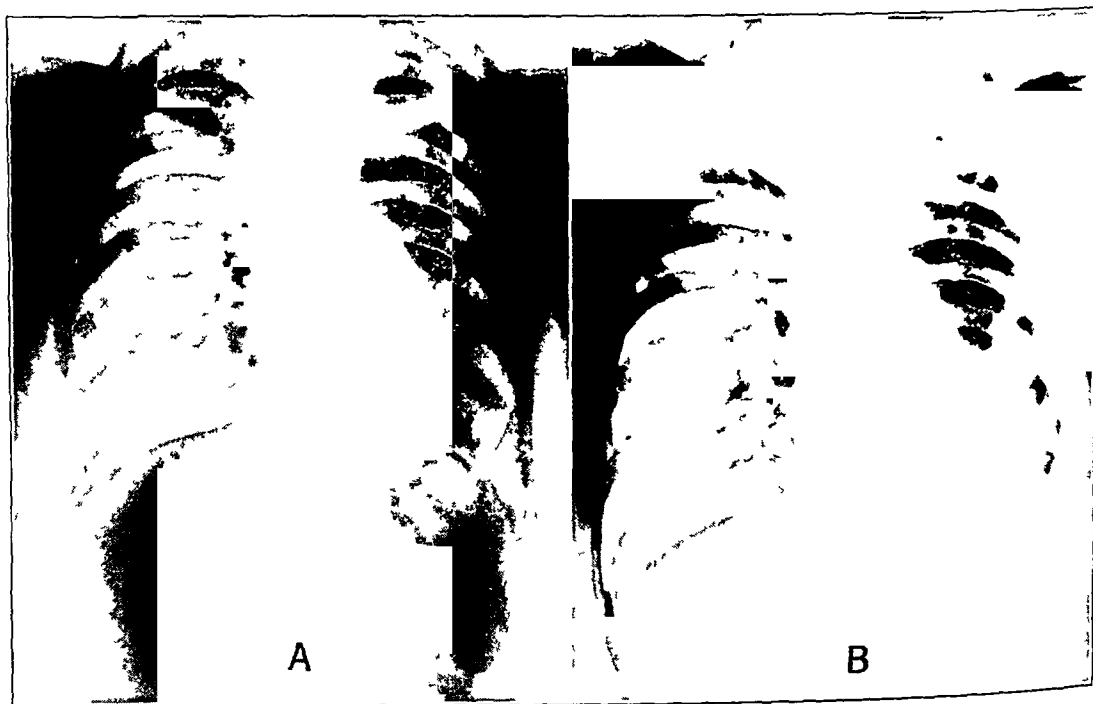


Fig 3 (E M) —A, case of far advanced bilateral pulmonary tuberculosis. Worse on the left side. B, seven days after phrenicectomy, showing rise of diaphragm. The patient had shown some clinical improvement.

In one case phrenicectomy was done to release the pull of adhesions on the apex and middle lobe, to stop hemoptysis and to increase collapse. The hemorrhages were stopped, and the patient's condition improved.

At present four of these patients have improved and one is worse.

Group 3 consists of four cases of tuberculosis in which phrenicectomy was done as a complement to multiple intercostal neurectomy, one of which is illustrated in figure 3.

Expectation was fulfilled in all four in that there was definite paralysis and paradoxical movement of the diaphragm and in two cases a definite rise of the diaphragm. In one there was improvement after

phrenicectomy alone. All of the patients had far advanced tuberculosis, were not suitable risks for thoracoplasty and nothing was expected from the phrenicectomy alone.

At present one of these patients is well, two have improved and one is worse.

Group 4 consists of eleven cases of pulmonary tuberculosis in which phrenicectomy was used as an independent procedure. The expectation was fulfilled in nine and not in two, a percentage of 82. Figure 4 illustrates a case of this group.

Seven were cases of far advanced tuberculosis involving both lungs, in which pneumothorax could not be induced. In six of these phrenic-

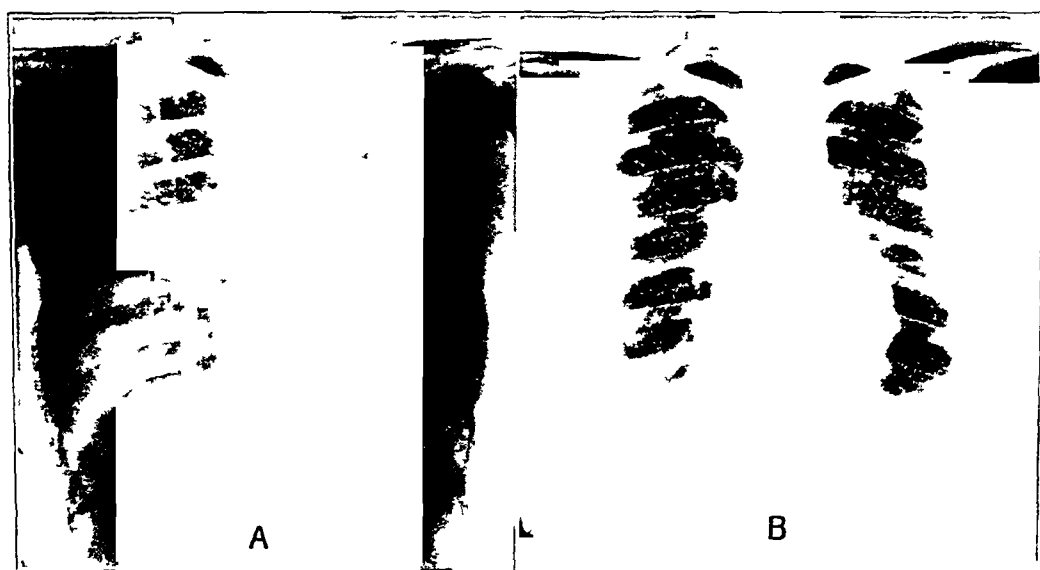


Fig 4 (A L)—*A*, far advanced bilateral pulmonary tuberculosis, worse on the left with a large amount of fibrosis. *B*, twenty months after left phrenicectomy, showing great improvement.

tomy was done to improve the worst side, in four there was improvement and in two there was not. In one case phrenicectomy was done on the worst side to stop repeated hemorrhages, which it did, and improvement followed.

One patient had early tuberculosis in both apices, and began to have repeated hemorrhages. A left phrenicectomy stopped the bleeding.

One patient had basal tuberculosis with a cavity in the lower lobe. Phrenicectomy greatly improved the lesion but did not quite close the cavity. pneumothorax was induced later.

Two patients had moderately advanced tuberculosis, for which phrenicectomy was done to control the lesions. Both have improved.

One patient with far advanced tuberculosis who was much improved on discharge became worse at home and died two months later.

At present two of these patients are well, five have improved, the condition of one is unchanged, two are dead and the result for one is unknown.

Group 5, represented by figure 5, consists of thirteen cases of bronchiectasis, of which five were right-sided, five left-sided, three bilateral but worse on one side, and two cases of fibrous pneumonitis.

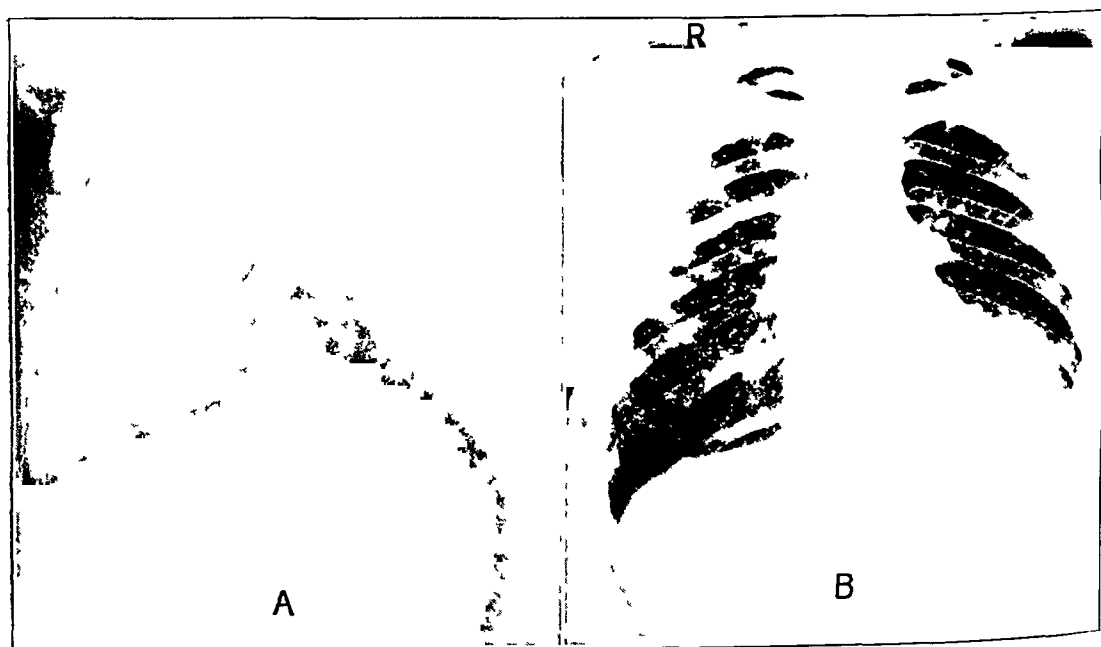


Fig 5 (G S) —A, a case of left basal bronchiectasis— injection of iodized oil B, three months after phrenicectomy, showing rise of diaphragm. There was great temporary improvement for three weeks, and the patient is now worse than before phrenicectomy.

The indications in three were palliation and as preliminary to thoracoplasty. In two there was moderate temporary improvement and in one slight temporary improvement, which was not lasting and thoracoplasty was performed.

In three patients the operation was done to supplement pneumothorax. Of these, one has improved slightly, the sputum being reduced 75 per cent, one has improved moderately for sixteen months and one improved moderately for several weeks, but required thoracoplasty later.

In four patients, phrenicectomy was done for palliation of bronchiectasis. One showed what was an apparent cure for two months and could be followed no longer, two showed slight temporary improvement

for a few weeks and then lost it, one showed great improvement for a few weeks and later became worse

In one case, the operation was done for palliation and as a preliminary to lobectomy. The patient showed great improvement for three weeks and then lost it. After a four-stage lobectomy he is now getting well.

In one case phrenicectomy was done to stop hemorrhages. The patient has had no more hemorrhages and has been greatly improved for eighteen months.

One indication was to relieve the pull on the mediastinum, to relieve dyspnea and as a prophylaxis against further dilatation of the bronchi. The patient has maintained great improvement for two years.

In one case of fibroid pneumonitis, phrenicectomy was done as prophylaxis against dilatation of the bronchi. The patient has been lost from observation.

One patient had a fibroid pneumoma and suffered from great pain due to diaphragmatic adhesions. She was temporarily relieved but the pain is now worse, ten months later.

In these fifteen patients, the expectation was fulfilled in eight, partly in three and not at all in four. Fourteen showed varying degrees of improvement, nine being only temporary. Five have held their improvement to date, the longest period being two years since operation. In only 35 per cent of the patients was improvement more than temporary.

At present five patients in this group have improved, the condition of three is unchanged, two are worse, three are dead and for two the results are unknown.

Group 6 consists of six cases of pulmonary abscess and four of chronic pulmonary suppuration.

In the cases of abscess phrenicectomy was indicated to stop hemorrhage and improve the abscess in one case, and to cure basal pulmonary abscess in one case. In both the results were unsuccessful, and in the latter thoracoplasty and cautery pneumonectomy were done later after which the patient recovered. In two cases temporary phrenicectomy followed by postural drainage cured abscesses of the left upper lobe. In one case it was done to cure pulmonary abscess, as the results were unsuccessful pneumothorax was then induced and was followed by great improvement. Five months later the patient was operated on by another surgeon and died. In one case phrenicectomy was done to cure abscess of the upper right lobe. Moderate temporary improvement followed lasting for three weeks then recrudescence of the abscess occurred and required surgical drainage. The patient is now well. Figure 6 illustrates a case of pulmonary abscess in which the patient was cured by phrenicectomy.

One patient in group 6 had a small chronic supradiaphragmatic empyema with a bleeding bronchopleural fistula. A phrenicectomy completely cured him.

In one patient, phrenicectomy was done for palliation of left basal chronic suppurative cavernous pneumonitis. Postural drainage was then instituted, and he is greatly improved five months later.

Phrenicectomy was done, after pneumothorax failed, as a preliminary to thoracoplasty on a patient with chronic pulmonary suppuration and subacute empyema. It was of no benefit, and the patient died after thoracoplasty.

In one case of chronic cavernous and suppurative pneumonitis phrenicectomy was done to stop repeated hemorrhages. This it did,

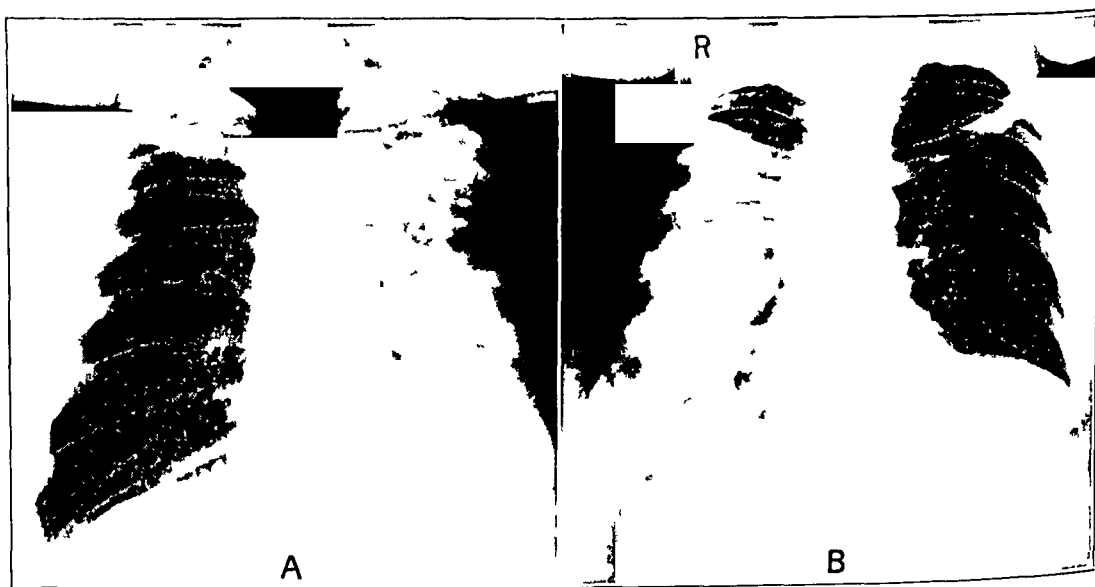


Fig 6 (L B) —A, case of pulmonary abscess of the left upper lobe. B, ten weeks after temporary phrenicectomy, showing rise of diaphragm. Abscess completely healed.

but subsequent drainage was required and the patient is now getting well.

The expectation was fulfilled in five of these ten patients. At present four patients in this group are well, three have improved and three are dead.

#### CONCLUSIONS

In evaluating the results of phrenicectomy in this series of cases, I have tried to determine in each instance whether phrenicectomy did what was expected of it or not. In pulmonary lesions, in which phrenicectomy was used as an independent procedure, improvement of the patient was the criterion for its success. However, in cases in which

phrenicectomy was used supplementary to thoracoplasty, intercostal neurectomy or pneumothorax, some of the patients did not show improvement from the phrenicectomy alone. The operation, however, was considered successful when the anatomic result (paralysis and rise of the diaphragm) did increase the compression obtained by thoracoplasty, the amount of relaxation of the lung produced by intercostal neurectomy and the degree of collapse in cases of artificial pneumothorax. The success or failure of compression therapy in these cases must rightly be credited to thoracoplasty, intercostal neurectomy or pneumothorax.

After analyzing a series of sixty-three cases with follow-up reports of sixty, it is found that phrenicectomy fulfilled its expectation in 75 per cent of a wide variety of pulmonary diseases. As alleviation rather than cure was the most that could be expected in a great majority of cases, it was necessary to employ further surgical procedures. From the experience of the surgical department of the University Hospital I have drawn several conclusions, as follows:

- 1 Phrenicectomy is a procedure of definite value in the surgical treatment for pulmonary diseases. It has numerous indications, but in a large majority of instances, it will be only a step in the surgical intervention of various pulmonary lesions, and one must be prepared to proceed with further measures when indicated.

- 2 Its widest field of application is in the treatment for predominantly unilateral pulmonary tuberculosis.

I believe that it should be used preliminary to every extrapleural thoracoplasty.

As a supplement to artificial pneumothorax therapy, I believe that it definitely enhances the value of this form of treatment, and will change many cases of unsatisfactory collapse into satisfactory ones. I believe that it should be used much more frequently than is the general custom.

Combined with multiple intercostal neurectomy, phrenicectomy offers a chance for cure in a small number of patients in whom pneumothorax or thoracoplasty should not or cannot be done.

As an independent procedure in the treatment for pulmonary tuberculosis, its indications are rapidly growing. In selected cases one can expect improvement from phrenicectomy alone in 80 per cent.

- 3 In bronchiectasis one may occasionally obtain a brilliant cure but as a rule the most that can be expected of phrenicectomy is improvement that is not permanent. In early cases of unilateral disease phrenicectomy combined with subsequent postural drainage is the treatment of choice. I believe that it should be seriously considered as a prophylaxis against bronchiectasis in every case of so-called fibroid pneumonia.

Patient	Age	Sex	Diagnosis	Indication	Operation and Date	Paralysis and Paradoxical Movement of Diaphragm, Period Since Operation	Rise of Diaphragm, Period Since Operation	Chronic Effect of Phrenicectomy	Subsequent Treatment
GROUP 1—Preliminary to Thoracoplasty—Far Advanced Pulmonary Tuberculosis									
F B	26	♀	Far advanced tuberculosis with fibrosis, mainly on left	Preliminary to thoracoplasty	Left phrenicectomy 1/8/25	Yes + 1 month	10 cm 1 month	Slight improvement	Two stage thoracoplasty, February, 1925
R F	30	♂	Far advanced tuberculosis of left apex with cavity	Preliminary to thoracoplasty	Left exeresis 12/31/26	Yes + 6 days	6 cm 6 days	Slight improvement	Two stage thoracoplasty January 1927
R M R	29	♂	Far advanced tuberculosis of left apex, with cavity, early lesion of right apex	Preliminary to thoracoplasty	Left phrenicectomy 2/20/26	Yes + 3 days	2 cm 3 days	Slight improvement	Two stage thoracoplasty March, 1926
L N	24	♀	Far advanced fibrotic tuberculosis of right lung	Preliminary to thoracoplasty	Right exeresis, 10 cm 5/22/25	Yes + 5 days	2 cm 5 days	No improvement	Two stage thoracoplasty, June, 1926
G M L	26	♀	Far advanced tuberculosis of left lung, healed lesion of right apex, tuberculous salpingitis and peritonitis	Preliminary to thoracoplasty	Left exeresis, 10 cm 4/9/26	Yes + 7 days	5 cm 7 days	No improvement	Two stage thoracoplasty May, 1926
D G F	43	♂	Far advanced tuberculous cavitation of right side	Preliminary to thoracoplasty	Right exeresis, 35 cm 5/17/27	Yes + 5 days	5 cm 5 days	No improvement	Two stage thoracoplasty June 1927 date July 29, 1927
C R S	22	♂	Far advanced tuberculosis of right lung with cavity, small lesion of left apex	Preliminary to thoracoplasty	Right exeresis 12 5 cm 1/30/28	Yes + 3 weeks	3 cm 3 weeks	Improvement	Improved for a while, pneumothorax attempted and failed two stage thoracoplasty, June 1
E K	26	♀	Chronic tuberculosis of left lung with pleural effusion	Preliminary to thoracoplasty	Left phrenicectomy 3/2/27	No Indeterminate	Indeterminate	No improvement	Three stage thoracoplasty March April 1
G W L	21	♂	Chronic left pulmonary tuberculosis with pleural effusion, tuberculous enteritis	Preliminary to thoracoplasty	Left exeresis 10/31/27	Yes + 1 day	1 cm 1 day	Improvement	Two stage thoracoplasty November, 1927
O F	23	♂	Chronic pulmonary tuberculosis with tuberculous empyema of left side	Preliminary to thoracoplasty	Left phrenicectomy 5/5/28	No Indeterminate	Indeterminate	No improvement	Four stage thoracoplasty May June 1928
D B	28	♂	Far advanced fibrotic tuberculosis of left lung	Preliminary to thoracoplasty	Left exeresis 34 cm 8/15/28	Yes + 1 week	2 cm 1 week	No improvement	Two stage thoracoplasty September, 1928
E Y	24	♀	Chronic bilateral tuberculosis right tuberculous empyema	Preliminary to Schede thoracoplasty	Right phrenicectomy 8/30/28	No Indeterminate	Indeterminate	No improvement	Three-stage thoracoplasty October 1928
B D H	27	♂	Chronic tuberculosis of right lung with complete tuberculous empyema	Preliminary to Schede thoracoplasty	Right phrenicectomy 12/21/28	Yes Yes 1 day	2 cm 1 month	Improvement, relieved from cough and pain	Three stage thoracoplasty February, 1929
G A	36	♀	Chronic tuberculosis of left lung with cavity left tuberculous empyema	Preliminary to thoracoplasty	Left exeresis, 37 5 cm 6/22/28	No Indeterminate	Indeterminate	No improvement	Three-stage thoracoplasty November, 1928
I O	19	♂	Far advanced tuberculosis of left lung with cavity	Preliminary to thoracoplasty	Left exeresis, 8 cm 8/3/28	Yes + 6 days	6 cm 6 days	Improvement	Two stage thoracoplasty September 1
G H	24	♀	Far advanced tuberculosis of left lung with cavity	Preliminary to thoracoplasty	Left exeresis 12 cm 7/23/28	Yes + 7 days	5 cm 7 days	Improvement	Two stage thoracoplasty December 1
E L	21	♀	Far advanced tuberculosis of left lung with cavity and pyopneumothorax	Preliminary to thoracoplasty	Left phrenicectomy 11/21/28	Yes + 7 days	Indeterminate	Improvement	Three-stage thoracoplasty February 1
I M	40	♀	Far advanced tuberculosis of left lung with cavity	Preliminary to thoracoplasty	Left exeresis 23 cm 12/15/28	Yes + 6 days	15 cm 6 days	No improvement	Two stage thoracoplasty February 1
GROUP 2—Supplementary to Artificial Pneumothorax—Cases of Pulmonary Tuberculosis									
I E K	20	♀	Moderately advanced pulmonary tuberculosis tuberculous colitis	To supplement pneumothorax to stop movement of right side of diaphragm and to lengthen interval between refills	Right phrenicectomy 5/3/27	Yes + 2 mo	3 5 cm 2 mo	Improvement	Pneumothorax stopped after year of treatment

\* The following abbreviations and symbols are found in the table ♀ female ♂ male SI slight Occ, occasional

Signs and Symptoms															Condition of Patient on Last Report	Comment
Cough		Amount of Sputum			Ease of Expectoration			Dyspnea			Temperature Fahrenheit					
Before	After Phrenicotomy	On Admission	After Phrenicotomy	On March 1, 1929	On Admission	After Phrenicotomy	On March 1, 1929	On Admission	After Phrenicotomy	On March 1, 1929	On Admission	After Phrenicotomy	On March 1, 1929			
GROUP 1—Preliminary to Thoracoplasty—Fair Advanced Pulmonary Tuberculosis																
		Slight		0			Easier	Yes		0	99		98.6	Well	Marrned later one child 15 mo old	
1	Mod	No	300 cc.	0				Yes	No	99	99	98.3	Well	Works 8 hours a day moderate exercise		
ere		None	50 cc	None			No difference	Yes	Yes	No	99	99	98.6	Well 3 years	Works 8 hours a day for 2 years skates skis	
re		Slight	300 cc	50 cc				Yes	Sl	100	100	98.6	Improved	Marrned		
l		None		15 cc			Easier	Yes	No	100	100	98.6	Well	Taught last year found it strenuous		
re			450 cc					Yes	Yes		100	99	Died	Cause of death military tuberculosis ball thrombus left side of heart		
re	Less severe	Slight	400 cc	90 cc	15 cc		More difficult	Yes	Yes	No	99	99	98.6	Well	Works as salesman	
								Yes	Yes		101	101	Died	Died on 4/23/27 of tuberculous meningitis		
	Less	None	150 cc	75 cc	0			Yes	Yes	Yes	99	99.6	98.6	Improved	Still on cure	
t	Slight	No		0	0				No	99	99	98.6	Improved	Still on cure		
	Slight	None	90 cc	60 cc	0		Easier	Yes	Yes	No	100	98.8	98.4	Improved	Gained 20 pounds still on cure but much improved 6 mo after operation	
	Slight		0	0			No change	Yes	Yes		99	99	Died	Died of influenza pneumonia 3 mo later		
	Slight	Slight	10 cc	10 cc	10 cc	Difficult	Easier	Easier	Yes	Yes	Yes	101	101	100	Improved	Not yet well after Schede thoracoplasty
	Mod	Slight	30 cc	30 cc	5 cc	Easy	Easy	Easy	Yes	Yes	Yes	99.6	99.6	98.6	Improved	Still on cure 4 mo after thoracoplasty
	Better	0	240 cc	180 cc	30 cc	Easy	Easy	Easy	No	No	No	99	98	98	Improved	Still on cure
	Mod	Slight	50 cc	5 cc	5 cc		Easier	Easy	Yes	Yes	No	98.6	98.6	98.6	Improved	Still on cure
	Mod	Severe	90 cc	60 cc	200 cc	Severe	Easy	Severe	Yes	Yes	Yes	100.6	99	102	Worse	Intant has developed spread in right lung
	Mod	Mod	15 cc	15 cc	30 cc		No difference		Yes	Yes		98.6	98.6	Died	Died 17 day after thoracoplasty from spread to right lung	
GROUP 2—Supplementary to Artificial Pneumothorax—Cases of Pulmonary Tuberculosis																
1	Less	None	0	0				Mod	Mod	Sl	98	98.6	98.6	Improved	Lung allowed to re-expand 1 year after phrenicotomy condition good no signs of activity	

c Imp improvement Temp temporary



Patient	Age	Sex	Diagnosis	Indication	Operation and Date	Fulfillment of Expectation	Paralysis and Paradoxical Movement of Diaphragm, Period Since Operation	Rise of Diaphragm, Period Since Operation	Clinical Effect of Phrenicectomy	Subsequent Treatment
J J S	37	♂	Far advanced tuberculosis, mainly on left with cavitation, diabetes	To supplement pneumothorax and to increase collapse of left lung	Left exeresis 35 cm 10/4/27	No	+ 10 days	6 cm 12 mo	Temporary slight improvement	Continuance of pneumothorax and rest
M L B	22	♀	Far advanced tuberculosis, mainly on right	To supplement pneumothorax, to release pull of adhesions at apex and middle lobe and to stop hemoptysis	Right phrenicectomy 10/24/28	Yes	+ 1 day	Indeterminate	Improvement	Continuance of pneumothorax and rest
Mrs T B	26	♀	Far advanced tuberculosis of right lung	To supplement pneumothorax and to increase collapse	Right exeresis 11.5 cm 10/29/28	Yes	+ 1 day	Indeterminate	Improvement	Continuation of pneumothorax and rest
B L H	51	♀	Far advanced tuberculosis of left lung	To supplement pneumothorax and to obtain greater collapse	Right phrenicectomy 10/24/28	Yes	+ 1 day	Indeterminate	Improvement	Continuation of pneumothorax and rest

## GROUP 3—Supplementary to Intercostal Neurectomy—Cases of Pulmonary Tuberculosis

Mrs I W	56	♀	Far advanced pulmonary tuberculosis, mainly on right side with cavitation	Preliminary to multiple intercostal neurectomy after failure to induce pneumothorax	Right phrenicectomy 10/27/27	Yes	+ 1 mo	Indeterminate 1 mo	No improvement	Multiple intercostal neurectomy of nerves 2 to 9 on right side, 11/2/28
M B	28	♀	Far advanced tuberculosis, mainly on left	Preliminary to multiple intercostal neurectomy after failure of pneumothorax therapy	Left exeresis, 7 cm 11/11/27	Yes	+ 2 mo	3 cm 2 mo	Slight improvement	Multiple intercostal neurectomy of nerves 2 to 10 2/2/28
E W M	17	♂	Far advanced pulmonary tuberculosis, mainly on left	Preliminary to multiple intercostal neurectomy	Left exeresis 25 cm 8/24/28	Yes	+ 7 days	4 cm 7 days	No improvement	Multiple intercostal neurectomy of nerves 2 to 11 9/1/28
M L McG	27	♂	Far advanced pulmonary tuberculosis, mainly on left side, cavitation, tuberculous laryngitis, tuberculous enteritis	Preliminary to multiple intercostal neurectomy	Left phrenicectomy 6/23/28	Yes	+ 3 days	Indeterminate 3 mo	No improvement	Multiple intercostal neurectomy of nerves 2 to 11 6/29/28

## GROUP 4—Independent Operations for Pulmonary Tuberculosis

H J H	29	♂	Chronic bilateral pulmonary tuberculosis, cavity of upper right been on cure 6 years	To improve right and to test left side	Right exeresis 12.5 cm 11/10/27	Yes	+ 2½ yr	5.5 cm 2½ yr	Improvement	Rest
Mrs A A L	27	♀	Far advanced tuberculosis of left lung, cavitation (?) some involvement of right lung	To stop repeated hemoptyses	Left exeresis 12/17/26	Yes	+ 6 mo	4.5 cm 6 mo	Improvement	Rest
G L	24	♂	Far advanced tuberculosis cavitation on left, moderately advanced on right, regressive	To control progressive lesions	Left phrenicectomy 10/26/28	Yes	+ 2 mo	2.5 cm 2 mo	Improvement	Rest
Mrs R M S	25	♀	Early tuberculosis of both apices	To control hemoptysis	Right exeresis, 25 cm 10/7/28	Yes	+ 3 mo	5 cm 3 mo	Improvement	Partial rest
H I B	14	♀	Progressive bilateral pulmonary tuberculosis worse on left	To control progressing left lesions	Left temporary phrenicectomy 11/16/28	No	+ 4 days	2 cm 2 mo	Temporary improvement	Rest

*Such Operations If Done—Continued*

Signs and Symptoms														
Cough			Amount of Sputum			Ease of Expectoration			Dyspnea			Temperature Fahrenheit		
On Admission	After Phrenicectomy	On March 1, 1929	On Admission	After Phrenicectomy	On March 1, 1929	On Admission	After Phrenicectomy	On March 1, 1929	On Admission	After Phrenicectomy	On March 1, 1929	On Admission	After Phrenicectomy	On March 1, 1929
Worse	Less	Slight	90 cc	60 cc	60 cc	Easier	Easier	No	No	No	No	98.6	98.6	98.6
												Worse		Improved for a while spread to other lung now pyopneumothorax
Mod	Less	Slight	30 cc.		0			Yes	Yes	Yes	Yes	98.6	98.6	98.6
												Improved		Still on cure much improved
					0			Sl	Sl	Sl	Sl	99	99	98.6
												Improved		Still on cure
					0			Sl	Sl	Sl	Sl	99	99	98.6
												Improved		Still on cure
GROUP 3—Supplementary to Intercostal Neurctomy—Cases of Pulmonary Tuberculosis														
Worse		Slight	120 cc		10 cc	Easier	Yes	Yes	Yes	Yes	Yes	99.4	99	98.6
												Well		Writes that she is well and working
Mod	Less	None		Less	2 cc			Yes	Yes	Yes	Yes	98.6	98.6	98.6
												Improved		Still on cure is greatly improved and considers herself well
Mod		Slight	60 cc		None							99	99	98.6
												Improved		Still on cure
Mod	No difference	Mod	60 cc	60 cc	150 cc	Difficult	Difficult	More difficult	Mod	Mod	Sl	100	100	99.6
												Worse		Still on cure worse
GROUP 4—Independent Operations for Pulmonary Tuberculosis														
Mod	Imp	Slight	60 cc	30 cc	30 cc	No difference		Yes	Worse	Same	Same	99	99	98
									for a while	as at first				Improved
														Still on cure reexamined March 1, 1929 showed cavity 1/2 former size both lungs much improved general condition improved
Mod	Imp	None		Decreased	0			No	No	No	No	100	99	9.6
												Improved		Occasional light housework clinically arrested
			180 cc	120 cc		Easier		Yes	Yes			99.4	98.3	
												No report		Transferred to another sanatorium 3 mo after phrenicectomy
Mod	None	None	None	None	None			Occasional	Occasional	Occasional	Occasional	98.6	98.6	98.6
												Improved		No hemoptysis x-rays show clearing feels well light housework
Mod	Slight	None	5 cc	cc	cc	Easier		No	No	No	No	98.6	98.6	98.6
												Unchanged		Still on cure some roentgen clearing on right and left

Patient	Age Sex	Diagnosis	Indication	Operation and Date	Fulfillment of Expectation	Paralysis and Paradoxical Movement of Diaphragm, Period Since Operation	Rise of Diaphragm, Period Since Operation	Clinical Effect of Phrenicectomy	Subsequent Treatment
D A	28 ♂	Far advanced tuberculosis of both lungs worse on left with cavities	To control extensive left lesions	Left temporary phrenicectomy 11/16/28	Yes	+ 2 mo	9 cm 2 mo	Improvement	Rest
W A	63 ♂	Far advanced tuberculosis, mainly on left with cavity tuberculosis of knee	To control extensive left lesions after failure to induce pneumothorax	Left phrenicectomy 11/18/27	Yes	+ 1 year	8 cm 1 year	Improvement	Rest
J Q	63 ♂	Far advanced tuberculosis, more on left (Indian)	To control progressive left lesions	Left phrenicectomy 2/11/27	No	+ 2 days	8 cm 2 mo	No improvement	Rest artificial pneumothorax attempted
C F F	38 ♂	Moderately advanced tuberculosis of right lung, diabetes	To control lesions after failure to induce pneumothorax	Right phrenicectomy 8/8/28	Yes	+ 2 mo	4 cm 2 mo	Improvement	Rest
Mrs A T	35 ♀	Right basal tuberculosis with cavity	To control right basal lesion	Right excision 2/16/27	Yes partly	+ 3 mo	7 cm 3 mo	Improvement	Rest, artificial pneumothorax to finish closing cavity on May 3, 1929
Mrs E C P	27 ♀	Moderately advanced tuberculosis of left lung	To control left lesions after induction of pneumothorax failed	Left excision 32 cm 11/10/27	Yes	+ 1 day	Indeterminate	Improvement	Rest
GROUP 5—Cases of Bronchiectasis									
G K	♂	Bronchiectasis of right lower lobe	Bronchiectasis	Temporary right phrenicectomy 11/1/20	Yes	+ 7 days	Indeterminate films lost	Excellent improvement	Postural drainage
Mrs D W	63 ♀	Bronchiectasis of left base	To supplement pneumothorax therapy	Left phrenicectomy 10/5/27	Yes	+ 5 days	7 cm 5 days	Moderate improvement	Postural drainage
Geo C	26 ♂	Extensive bronchiectasis of left lung	Preliminary to thoracoplasty	Left phrenicectomy 5/9/27	Yes	+ 1 day	Indeterminate	Moderate improvement temporary	Several stage thoracoplasty Aug to Oct 1927, cautery pneumonectomy January, 1928
H S S	19 ♀	Bilateral bronchiectasis mainly of right	Palliation of bronchiectasis	Right phrenicectomy 11/30/27	No	+ 4 days	2 cm 8 mo	Slight improvement, temporary	Postural drainage
A L V	59 ♂	Left hilar bronchiectasis arteriosclerosis myocarditis	Palliation	Left temporary phrenicectomy 5/15/28	No	+ 2 days	3 cm 1 mo	Great improvement, temporary	Postural drainage
Mrs M T	34 ♀	Chronic bilateral basal bronchiectasis mainly on left	Palliation	Left excision 10 cm, and cut nerve to sub c 6/27/28	Partly	+ 2 days	Indeterminate 3 mo	Slight improvement temporary	Postural drainage
G S	19 ♂	Bronchiectasis of left lower lobe	Palliative and preliminary to lobectomy	Left excision 9/26/28	Yes	+ 2 mo	2 cm 2 mo	Great improvement, temporary	Four stage lobotomy, Dec. 1927 to Feb., 1929
D J A F	27 ♂	Left bronchiectasis seen left pulmonary fibrosis	Prophylaxis against further dilatation of bronchi	Left phrenicectomy 3/5/28	?	+ 4 days	2 cm 4 days		
Mrs M A B	47 ♀	Painful right diaphragmatic adhesions right basal fibrous pneumonitis	Prophylaxis against bronchiectasis and to relieve pain from diaphragmatic adhesions	Right phrenicectomy 5/17/28	No, except temporary relief	+ 7 days	3 cm 7 days	Temporary	

Signs and Symptoms																
Cough			Amount of Sputum			Ease of Expectoration			Dyspnea			Temperature Fahrenheit			Condition of Patient on Last Report	Comment
On Admission	After Phrenicectomy	On March 1, 1929	On Admission	After Phrenicectomy	On March 1, 1929	On Admission	After Phrenicectomy	On March 1, 1929	On Admission	After Phrenicectomy	On March 1, 1929	On Admission	After Phrenicectomy	On March 1, 1929		
mod									No	No	No	99	98.6	92.6	Improved	Wife writes that he is improved
mod	Imp		150 cc	100 cc					Yes	Yes		100	99		Died	Died on Feb 27 1929
vere	No change		200 cc	200 cc					Yes	Yes		101	101		Died	Died 3 mo after phrenicectomy
	Slight		0	10 cc	240 cc							100	99.4		Improved	Vomited 1 week after phrenicectomy no note since discharged on Oct 1 1925
mod			150 cc	25 cc	0				No	No	No	101	100	98.6	Well	Does light house work
mod	Less	None		Less	None				Sl	Sl	No	99	98.6	98.6	Well	Works 7 hours a day considers herself well
GROUP 5—Cases of Bronchiectasis																
ere	None		400 cc	0					No	No		99	98		Improved 2 mo later	Followed for 2 mo unable to locate
d		No	160 cc		40 cc			Easier	No	No	No	98.6	98.6	98.6	Improved	Still on continuous postural drainage
ere	Severe	Mod	600 cc	300 cc	240 cc			Harder	Yes	Yes	Yes	99	99	98	Improved	Not well able to do some work bronchopleural fistula
d	Imp	Imp	90 cc	160 cc 2 mo later	90 cc			Easier	Yes	Yes	Yes	99	99	98.6	Unchanged	General condition has improved
ere	Mod	Severe	240 cc	30 cc 1 mo	240 cc			No difference	Yes	Yes	Yes	99	99	99	Worse	In hospital much worse pain weakness cough
d	Mod	Mod	120 cc	200 cc 1 mo	80 cc			Easier	Yes	Yes	Yes	100	99	99	Unchanged	No change considers herself improved return of function of diaphragm
ere	Temp imp	Slight	160 cc	40 cc 2 wk 300 cc 2 mo	5 cc			Easier	Yes	Yes	Yes	Frequent rle	98.6	98.6	Improved	Now up and about condition rapidly improving has bronchial fistula to be closed at later date
ic	None		0	0					No	No		99	99			No report
	No	No	0	0	0				0	0	0	99.2	99	98.6	Worse	Patient writes that she is worse

Patient					Paralysis and Rise of Paradoxical Movement of Diaphragm, Since Operation		Fulfillment of Expectation		Clinical Effect of Phrenicectomy		Subsequent Treatment	
Age	Sex	Diagnosis		Indication	Operation and Date	Operation	Period Since Operation	Operation	Period Since Operation	Phrenicectomy	Treatment	
O K 44 ♂		Bronchiectasis	suppurative pneumonitis lung abscess	To supplement pneumothorax therapy	Right phrenicectomy 12/4/26	Yes for a while	+	10 days	2 cm	10 days	Temporary	Rib resection and drainage pulmonary abscess 1/26/27
E M H 22 ♀		Bilateral bronchiectasis mainly on left		Palliation and is preliminary to thoracoplasty	Left phrenicectomy 2/7/27	Yes	+	7 days	3 cm	7 days	Moderate improvement, temporary	First stage thoracoplasty, 3/1/27, appendectomy, 4/4/27
W M C 22 ♂		Right bronchiectasis	right lung abscess	Palliation and a preliminary to thoracoplasty	Right exeresis 6/2/28	Yes	+	2 days	5 cm	2 days	Slight improvement, temporary	Three-stage thoracoplasty, August, 1928
H M 29 ♂		Syphilis	left fibrous pneumonitis, atelectasis and bronchiectasis	To relieve pull on mediastinum, to relieve dyspnea, and as prophylaxis against further embarrassment of heart	Left phrenicectomy 4/1/27	Yes	+	25 days	Indeterminate 25 days		Slight improvement	Antisyphilitic
M L S 17 ♀		Right bronchiectasis,	extensive	To supplement pneumothorax and to increase collapse	Right exeresis 12/10/28	Partly	+	2 weeks	Indeterminate 2 weeks		Slight improvement	Continuation of pneumothorax and rest
G M S 30 ♀		Bronchiectasis of middle lobe	mild	To check hemoptysis	Right exeresis 6/16/28	Yes	+	2 days	Rise indeterminate 3 mo		Great improvement	Rest for 4 months

## GROUP 6—Cases of Pulmonary Suppuration

M L C 61 ♀			Abscess of lung, right upper lobe, hemoptysis	For hemoptysis and treatment for lung abscess	Right phrenicectomy 5/26/26	No	+	7 days	5 cm	No improvement	Thoracoplasty, first stage 6/4/26, 2d stage 3/23/27
H A L 26 ♂			Chronic empyema with bleeding, bronchopleural fistula	To stop hemoptysis	Right exeresis 33 cm 2/3/27	Yes	+	10 days	Rise indeterminate	Great improvement	
W O 30 ♂			Lung abscess chronic nephritis, arteriosclerosis neuroretinitis, epilepsy	For right basal lung abscess	Right exeresis 24 cm 10/8/27	No	+	2 days	Rise 5 cm, 2 days	Slight improvement, temporary	Thoracoplasty and cauterization, pneumonectomy December, 1927, January, 1928
I O 39 ♀			Chronic right pulmonary suppuration with subacute empyema	After pneumothorax failed as preliminary to thoracoplasty	Right exeresis 1/14/28	No	Indeterminate	Indeterminate	No improvement		1/26/28 to 1/31/28 two stage exploratory thoracotomy 3/17/28 first stage thoracoplasty
S H D ♂			Abscess of upper left lobe of lung	For lung abscess	Temporary left phrenicectomy 6/16/28	Yes	+	8 days	3 cm	Great improvement	Postural drainage
L O B 28 ♂			Subacute abscess of lung upper left lobe	For lung abscess	Temporary left phrenicectomy 10/6/28	Yes	+	4 days	4 cm	Great improvement	Postural drainage
G L D ♂			Left basal chronic suppurative cavernous pneumonitis	Palliation	Left phrenicectomy 10/6/28	Yes	+	4 days	Indeterminate	Great improvement	Postural drainage
I R ♂			Abscess of right lower lobe of lung	Lung abscess	Temporary right phrenicectomy 7/21/28	No	+	1 week	3.5 cm	Slight improvement, temporary	Pneumothorax induced Aug 1 1928
I D 25 ♀			Lung abscess upper right lobe	Lung abscess	Temporary right phrenicectomy 10/2/28	No	+	2 days	2.5 cm	Moderate improvement temporary	Postural drainage two stage drainage of lung abscess December, 1928
I C 15 ♀			Left chronic pulmonary suppuration complicated by osteomyelitis of right femur	For severe hemoptysis	Temporary left phrenicectomy 1/7/29	Yes	+	1 week	Rise indeterminate	Slight improvement temporary	Drainage of abscess Feb 1929

Signs and Symptoms																	
Cough			Amount of Sputum			Ease of Expectoration			Dyspnea			Temperature Fahrenheit			Condition of Patient on Last Report	Comment	
On Admision	After Phrenl ectomy	On March 1, 1929	On Admision	After Phrenl ectomy	On March 1, 1929	On Admision	After Phrenl ectomy	On March 1, 1929	On Admision	After Phrenl ectomy	On March 1, 1929	On Admision	After Phrenl ectomy	On March 1 1929			
vere	Mod		450 cc.	200 cc			Easier					101	100		Died	Died 8 days after thoracotomy autopsy showed large lung abscess connecting with a bronchiectatic abscess	
vere	Severe		600 cc	150 cc			Easier					100	100		Died	Died of pneumonia on other side 30 days after thoracoplasty	
vere			250 cc	150 cc								98.6	98.6		Died	Died 25 days after last stage thoracoplasty	
mod	Less	Mod	60 cc.	30 cc	60 cc		More difficult	Mod	None	None	98.6	98.6	98.6		Improved	Two years later patient states he is well	
ght	Slight	Slight	60 cc	15 cc	15 cc		No difference		SI	SI	SI	98.6	98.6	98.6	Unchanged	Still in hospital	
ght	None	Slight	5 cc	5 cc	5 cc				No	No	No	99.2	99.2	98.6	Improved	Feels much better gained 10 pounds	
GROUP 6—Cases of Pulmonary Suppuration																	
ere	Severe											100	101		Died	Died of pulmonary hemorrhage 12 days after last thoracoplasty	
d	Imp	None	20 cc	0	0		Easier	Easy	Yes	No	No	99	98.6	98.6	Well	Well 2 years later works no hemorrhages since phrenl ectomy	
d	Temp imp	Slight	200 to 300 cc	100 to 200 cc	5 to 10 cc		More difficult	More difficult	Yes			Occ	102	100	98.6	Improved	Patient is free from lung abscess has a broncho-cutaneous fistula is in hospital for treatment for nephritis
ere	Severe		500 cc						Yes			100	100		Died	Died 5 days after thoracoplasty	
re	Mod	0	400 cc		0		Easier		No	No	No	101	100	98.6	Well	Well chest clear by x-ray on Nov 9 1928	
l	Less	0	150 cc	70 cc	0		Easier		No	No	No	100	99	98.6	Well	X-ray checkup on Jan 29 1929 shows abscess healed well and working on March 1 1929	
re	Less	Mod	400 cc	100 cc	40 cc		Easier	No difference	Yes	No	SI	100	100	98.6	Improved	Last report March 1 feels much improved	
re	Less		800 cc.	200 cc								101	101		Died	Died 5 mo later following operation by another surgeon	
re	Temp imp	0	300 cc	Temp 0 reduction to 40 cc 3 wk	0		Easier		Yes	Yes	Yes	99.4	100	98.6	Well	Gained 20 pounds looks well still has a small cavity not yet filled in also bronchial fistula	
re	Mod	0	60 cc	60 cc	0		Easier		No	No	No	100	101	98.6	Improved	Lung condition has cleared up	

4 In subacute and chronic pulmonary abscesses after rest in bed and postural drainage have been tried, I believe that temporary phenicectomy will in selected cases allow the lung to relax enough to permit the cavity to contract and heal the lesion. It should receive more attention, in the treatment for pulmonary abscess, than is reported in the literature.

5 In cases of chronic pulmonary suppuration or suppurative pneumonitis, I do not expect a great deal of phenicectomy alone, but feel that it is a valuable procedure to be combined with other surgical measures.

# PAPILLOMAS OF THE CHOROID PLEXUS

REPORT OF TWO CASES, ONE WITH REMOVAL OF TUMOR AT OPERATION  
AND ONE WITH "SEEDING" OF THE TUMOR IN THE  
VENTRICULAR SYSTEM \*

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Papillomas of the choroid plexus are a well known but relatively uncommon tumor in neuropathologic literature and much rarer still in surgical literature. Two cases of a true papilloma of the choroid plexus of the left lateral ventricle are here reported. In one the tumor was removed in toto at operation and the other was encountered at autopsy. The latter is of especially great interest in that it represents an instance of "seeding" of this type of tumor throughout a portion of the ventricular system. Credence has not been given to "seeding" of papillomas of the choroid plexus though there are several descriptive cases in the literature.

## REPORT OF CASES

**CASE 1 (J. S.)**—*Solid vascular tumor of inferior medial wall of left lateral ventricle in an infant, aged 3 months. Roentgen treatment following disclosure of tumor at operation; reduction in size of tumor; excision in toto at second stage operation. Pathologically a true papilloma of the choroid plexus.*

**Clinical Record**—An infant, aged 3 months, was admitted to the surgical service on Sept. 3, 1928, because of bilateral internal squint and gradual enlargement of the head. The patient, a first child, was born at full term weighing 8½ pounds (3.8 Kg.). There was nothing of note in the birth record except slight difficulty in getting the patient to breathe following a normal delivery. Vomiting occurred several times at the age of 5 or 6 days, and hypodermoclyses of saline solution were given because of dehydration. At the age of 2½ months a left internal squint was noticed which cleared up in a day or so and then recurred shortly after, with an internal squint on the opposite side. This persisted up to the time of admission. About two weeks prior to entry the head was noted to be enlarging; the veins of the scalp to be more prominent and the fontanels to be bulging more than usual. Vomiting had occurred only once in this two week period and feedings had been taken about as usual.

**Physical Examination**—The patient was a well developed and well nourished active infant with a moderately enlarged head which measured 46 cm. in its greatest circumference and 30 cm. from the glabella to the external occipital protuberance. The fontanels were bulging moderately and the veins of the scalp were fairly prominent. The only cranial nerve palsies noted were a bilateral abducens of moderate degree. The left arm and leg did not seem to be moved.

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quite as much as the right though there was not any actual weakness noted. Deep reflexes on the left side were slightly increased over those on the right, neither observation was in keeping with subsequently disclosed conditions. On Oct 1, 1928, the right ventricle was tapped and clear fluid under increased tension escaped. Twenty cubic centimeters of a 1 per cent solution of indigo carmine was introduced into the ventricle, and the left ventricle was tapped a few moments later. On tapping the left ventricle, highly xanthochromic fluid, also under tension, escaped but no trace of the dye was encountered. A lumbar puncture done about a half hour later showed that a faint trace of the dye had reached the lumbar sac. Results of examination of the fluids appear in the accompanying tabulation.

*Operation*—On Oct 3, 1928, under ether anesthesia a left-sided bone flap was turned down. The surface of the brain showed much flattening of the convolutions especially in the temporal region. An incision was made in the postparietal region through the thinned cortex extending into the distended ventricle. On the medial wall of the ventricle, about opposite the pineal gland region there was seen an irregular tumor mass 5 or 6 cm in length and 4 or 5 cm in height. The surface was grayish red. Around this tumor was a delicate envelope which was rather closely adherent to it. The tumor appeared on inspection to be too vascular for biopsy.

	Right Ventricle	Left Ventricle	Lumbar Sac Fluid
Pressure	Increased	Increased	Normal
Cells	0	Many old crenated red blood cells	0
Randy reaction	+	+++	+
Total protein	225 mg	2,062 mg	240 mg
Chlorides	720	708	768
Sugar	43.5	54	57
Specific gravity	1.012	1.015	Insufficient
Bile salts	0	0	0
Wassermann reaction	Negative	Negative	Negative
Guinea pig inoculation	Negative	Negative	Insufficient

Consequently an opening about 1 cm in diameter was made through the septum pellucidum to allow fluid to escape into the opposite ventricle. A small decompression in the left subtemporal region was made. The patient made an uneventful recovery from the operation and was discharged on the tenth postoperative day.

*Roentgen Treatment*—The patient received deep roentgen treatments on Oct 16 and Nov 6, 1928, and on Jan 15, 1929. There was moderate vomiting after each of these treatments.

*Reentry*—On Feb 6, 1929, the patient was readmitted because of the slowly increasing size of the head in spite of the roentgen treatment. Otherwise the patient had developed normally, and had gained steadily in weight and strength. The head measured 52 cm in the greatest circumference, as compared with 46 cm on previous admission. There were no cranial nerve or pyramidal tract palsies. A right homonymous hemianopsia seemed certain from repeated examinations. The fontanels were under moderate tension.

*Operation*—On Feb 7, 1929, the left-sided craniotomy wound was reopened and the tumor exposed. There was at once apparent a striking change in its size and consistency. The tumor was firmer, appeared less vascular, and seemed to have decreased about 2 cm in size in all dimensions. On dissection around the base it was found to be connected with the choroid plexus. Excision in toto was accomplished with the aid of the electrocautery. The patient made a

good recovery from operation did not appear to have any pyramidal tract palsies and was again discharged on the tenth postoperative day

*Comment*—The anterior portion of the choroid plexus was left intact though it probably would have been better to have put a silver clip on its blood supply or to have excised it entirely

*Pathologic Examinations*—After hardening in a diluted solution of formaldehyde (10 per cent), the tumor measured 4.5 by 3 cm (fig 1) It was definitely delimited on all sides by a thin delicate membrane of glial tissue On cut section the granular papillary structure of the tumor could be made out Numerous minute cysts were encountered Two fairly large arteries could be seen going into the tumor at its base where it was connected with the choroid plexus Histologic examination of the tumor showed it to be a typical papilloma of the choroid plexus Each section showed myriads of papillary projections most of

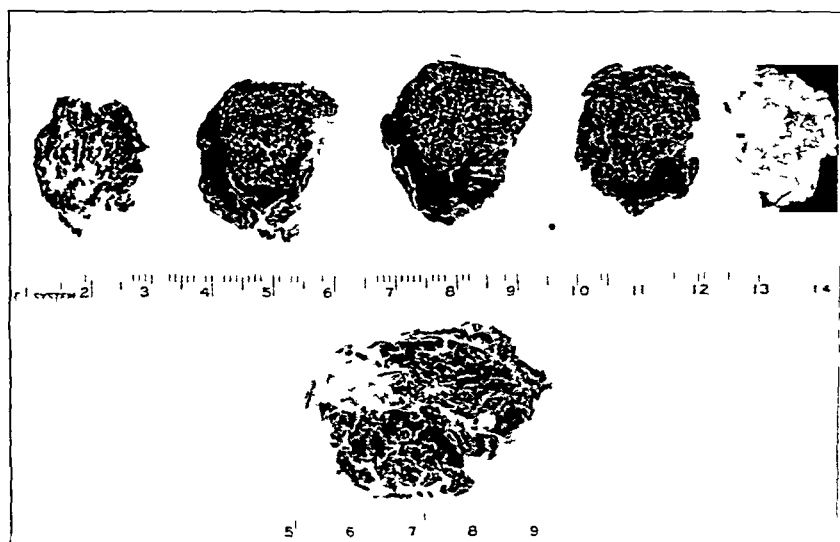


Fig 1 (case 1)—Cut surfaces of tumor, papilloma of the choroid plexus and tumor in gross

which had a connective tissue core, as demonstrated by van Gieson's and Perdrau's stains The papillae were covered for the most part by a single layer of cuboidal or columnar epithelium Pseudostratification occurred in some areas No cilia could be seen, and blepharoplasts could be demonstrated by either Ortega's silver carbonate or Bailey's ethyl violet orange G stain Glial fibers in the stroma of the tumor could not be made out (figs 2 and 3) The diagnosis was papilloma of the choroid plexus of the left lateral ventricle

*Clinical Course*—Since discharge now eight months ago the patient has continued to improve The head measures 49 cm in its greatest circumference as compared with 53 cm before the second operation and 46 cm before the first (fig 4) There are no pyramidal tract palsies A partial right homonymous hemianopia persists Growth has continued normally

*CASE 2 (I R)*—*Enormous papilloma of left choroid plexus filling entire left lateral ventricle and third ventricle. Seeding of tumor in temporal horn of left ventricle and one implant in right lateral ventricle.*

*Clinical Record*—The patient, a boy, aged 13, was admitted on the pediatric service in a critical state on June 25, 1927. He was suffering from headache, weakness of all extremities, aphasia, loss of weight, and pain and swelling in the region of the left knee joint. The father died at the age of 27, of pulmonary tuberculosis and tuberculous meningitis. The patient was exposed to infection from the father for eight years.

About fourteen months prior to admission the patient had an attack of "influenza" following which he tired easily. He became extremely "nervous," had trembling of the hands and feet, and found it increasingly difficult to walk or to handle objects. He continued to attend school until six months prior to entry. At this time his speech became markedly affected, he could not "get his words"

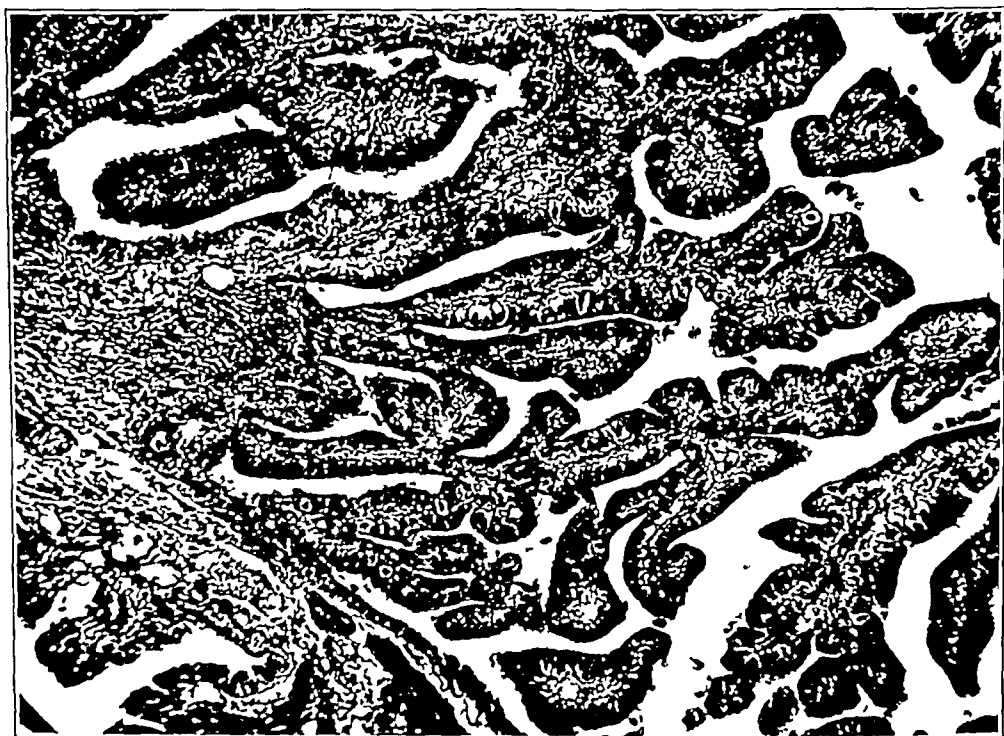


Fig 2 (case 1) —Papilloma of the choroid plexus showing the general architecture of the tumor, phosphotungstic acid hematoxylin stain, reduced from  $\times 150$

and was much confused. Headaches were severe. Three and a half months prior to entry he was confined to bed. He was observed in another hospital for three weeks where a polyuria as high as 3,900 cc a day, with an average of from 2,400 to 2,700 cc a day, was noted. A calcification to the left of the midline in the region of the pineal gland was demonstrated roentgenologically. Lumbar puncture showed a clear fluid "under tension," with 27 cells, globulin 3—. A diagnosis of tuberculous meningitis with polyuria was considered. In the interval between his stay at this hospital and admission to the Strong Memorial Hospital the course was progressively downward with added complaints of painful swollen joints. After about three months at home he was admitted to the hospital.

*Physical Examination*—On admission, the patient who was tall and much emaciated, was unconscious most of the time and comprehended little of what was going on about him. There was a cracked pot sound on percussion of the skull. The neck was stiff and there was a bilateral positive Kernig sign. The pupils were dilated and unequal the right being larger but both reacted slowly to light, there was a third nerve palsy on the left with external squint and nystagmus on looking to the right. The visual fields were impossible to map out. Ophthalmoscopic examination showed the veins to be tortuous and full and the disk margins hazy, without elevation of the disks. The optic cups were filled and the picture was one of a residuum of old choking of the disks. There was a right lower facial palsy, the gag reflex was absent and the pharynx muscles immo-



Fig. 3 (case 1)—Connective tissue framework of papilloma of the choroid plexus, Perdrau's connective tissue stain,  $\times 620$

bile. The tongue could not be protruded. All the deep reflexes were increased with a bilateral positive Babinski reflex, the ankle clonus varied from time to time. The superficial reflexes were absent. Roentgen examination showed a separation of the sutures, thinning of the bones and a calcified shadow in the region of the pineal gland about 2 cm. to the left of the midline.

*Clinical Pathology*—The urine was normal. The intake of fluid was from 1,200 to 1,500 cc. a day, but the output could not be accurately recorded the patient being incontinent. The reaction to the tuberculin test was positive with 0.1 mg. human I.D. The spinal fluid was clear, colorless and under "moderately increased pressure." The cell count was 13 with 4 polymorphonuclear leukocytes and 9 lymphocytes. The spinal fluid showed sugar 77 mg. per hundred cubic centimeters, and globulin definitely increased. The Wassermann reaction was

negative. The colloidal gold curve read 0000112211. The clinical course was steadily downward, and the patient died six days after admission.

Examination of the brain, which was fixed in a diluted solution of formaldehyde, showed the convolutions to be definitely flattened and widened with almost complete obliteration of the subarachnoid spaces, particularly on the left side. The whole left hemisphere was enlarged as compared with the right, and the median sulcus was seen to be deflected toward the right. On inspecting the base of the brain marked fullness was seen in the region of the pituitary and mammillary bodies, extending from the optic nerves back to the interpeduncular region. This was found to be a tumor which had extended into the third ventricle. It was covered by arachnoid and a thin film of glial tissue. The hypothalamic region was destroyed completely. The optic nerves were surrounded entirely. The

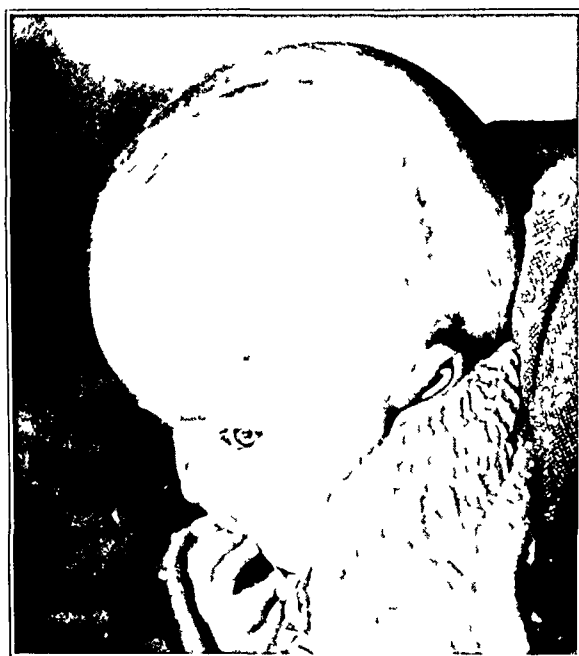


Fig. 4—Patient in case 1, two months following an operation

carotid arteries were pushed far to each side. The pituitary gland was removed for histologic study. In gross it appeared normal.

Beginning with frontal sections cut from the occipital pole forward, the first vestige of tumor was seen about 4 cm. from the tip of the occipital pole (figs. 5, 6, 7 and 8). This section showed a dilated ventricle on the right side and on the left a bit of tumor about 1 cm. long and 0.5 cm. wide. This was the posterior portion of a tumor which extended entirely through the left hemisphere to within 2 or 3 cm. of the frontal lobe. The tumor rapidly enlarged as it went forward, and sent finger-like processes short distances out into the brain substance, though everywhere these were sharply demarcated from the surrounding brain. There were areas in the tumor of a peculiar brownish translucent, fairly firm substance which looked like hardened colloid. In the region of the anterior portion of the cerebral peduncles the tumor reached the size of 7 cm. in transverse and 6.5 cm. in vertical diameter. In this same section the third ventricle could be seen to be

dilated, pushed toward the right side and filled with tumor tissue. In the next section forward, the third ventricle was better seen. Here again it was entirely filled with tumor which extended down into the region of the infundibulum and was separated from the arachnoid and the pituitary stalk only by a very thin

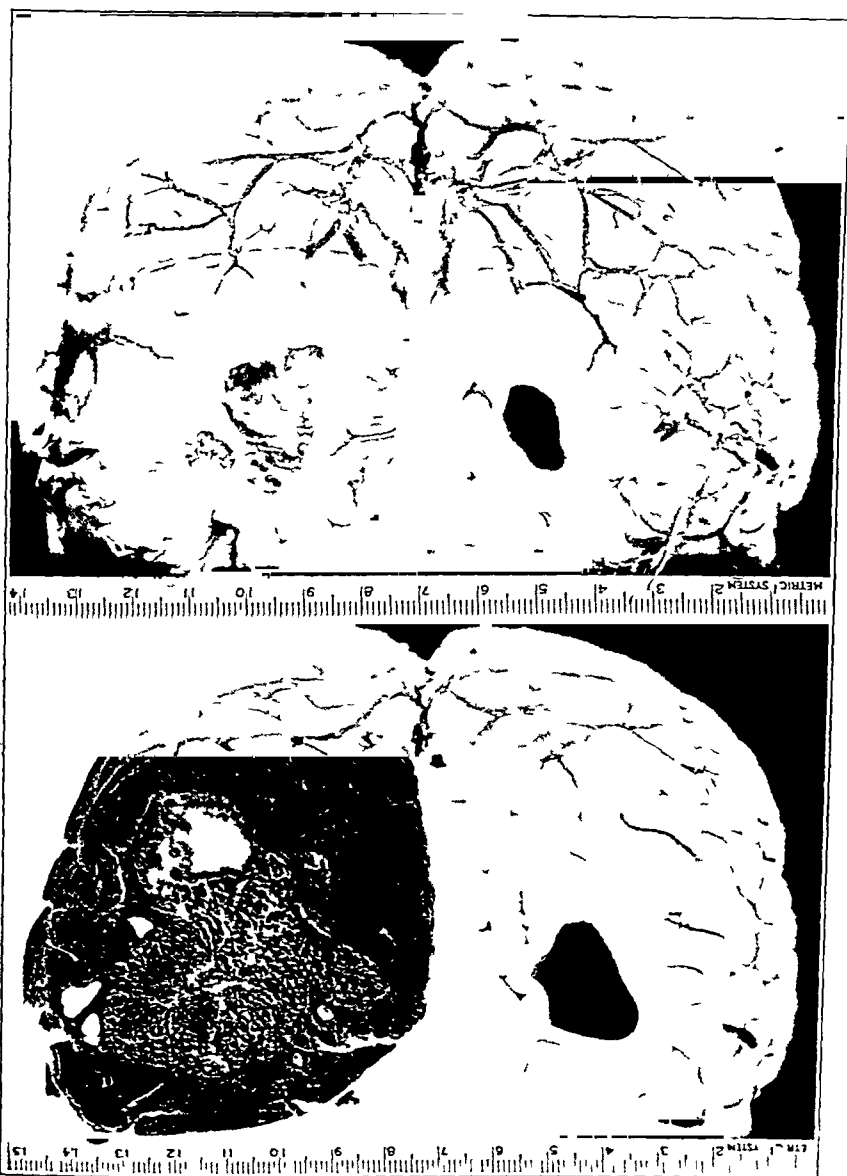


Fig 5 (case 2)—Papilloma of the choroid plexus of left lateral and third ventricles,  $\times 1$

shell of glial tissue. The left temporal horn was better seen in this section also. Its walls were studded with many small implants which had the same consistency as the tumor elsewhere. Direct implantation seemed without doubt to have taken place. There was also a portion of the temporal horn wall that was

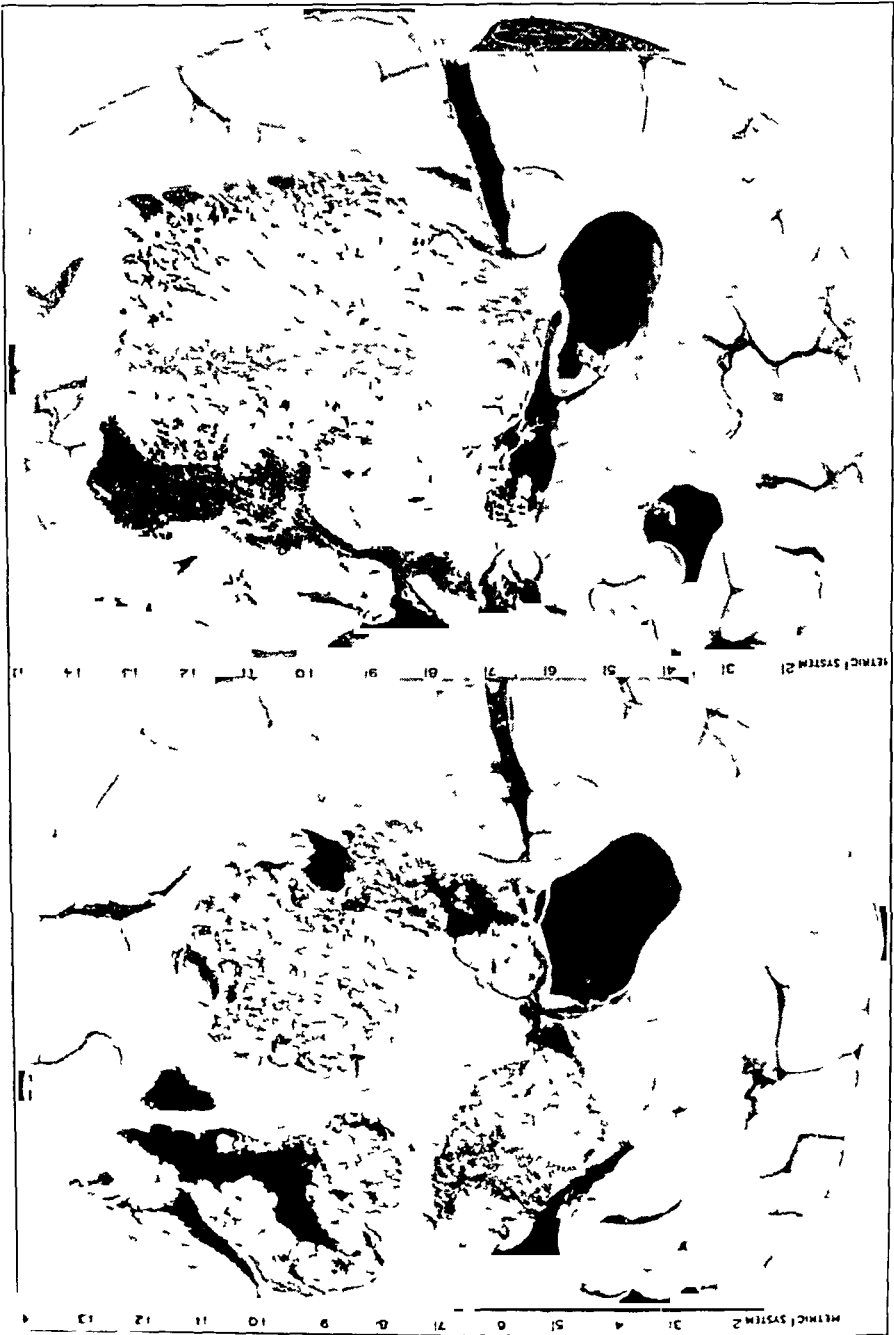


Fig 6—Sections of the papilloma shown in figure 5



Fig 7—Sections of the papilloma shown in figure 5



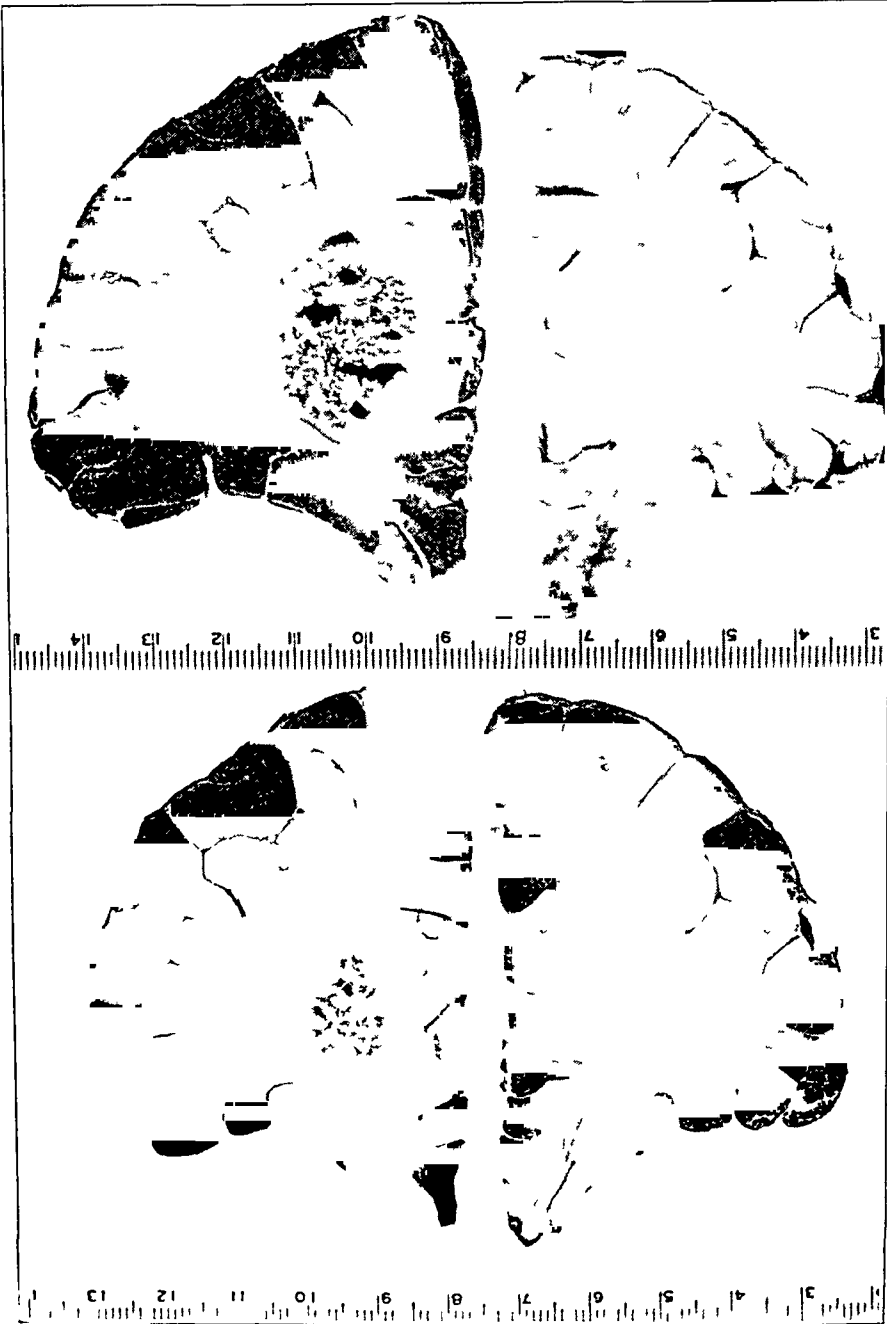


Fig 8—Sections of the papilloma shown in figure 5

covered with tumor which had grown in by direct extension. This same growth by implantation was also seen in the left anterior horn which was not as completely filled with tumor however as was the posterior or the temporal horn. Vestiges of the choroid plexus itself could not be made out except for a short distance in the anterior horn. As stated before the tumor extended forward to within 2 or 3 cm of the left frontal pole. In the main it was granular, it seemed to have a central core in places which looked like fibrous connective tissue. There was an apparent papillary arrangement in the larger portions of the tumor. There were many small cysts varying from 1 to 3 or 4 mm in diameter, with a few small necrotic zones. The choroid plexus on the opposite side appeared to be essentially normal. The opposite ventricle was much dilated. The fourth ventricle appeared



Fig 9 (case 2)—Tumor of the choroid plexus implanted on wall of right lateral ventricle, reduced from  $\times 3$

normal. The pituitary gland was entirely normal, both grossly and histologically. No evidences of the pineal gland could be made out.

In the opposite dilated occipital pole, entirely separate from any vestiges of the choroid plexus, there was a small raised papillary-like structure which was an implantation from the tumor of the opposite ventricle (figs 9 and 10).

*Microscopic Examination*—Blocks were taken from several parts of the tumor and showed the structure to be essentially the same everywhere. There were many papillae varying in size from short thick structures to long slender filaments, some of which represent side branches from the papillae. The core was of connective tissue as demonstrated by van Gieson's and Perdrau's stains (fig 11). The epithelium varied from low cuboidal to high columnar and was single-layered in nearly all instances. A few areas of pseudostratification were seen. Mitoses were

not made out. Blepharoplasten could not be demonstrated by either Hortege's silver carbonate or Bailey's ethyl violet orange G stain. Glial fibers could not be demonstrated in the core of the tumor. Numerous cysts were found in the tumor, all of which were formed by a colloid degeneration of the connective stroma of the papillae.

#### REVIEW OF THE LITERATURE

Mallory<sup>1</sup> has called attention to a method, based on earlier histologic studies of the ependyma, of accurate differentiation of ependymal from



Fig 10 (case 2)—A, implanted seed of tumor of choroid plexus—occipital horn of the right ventricle, phosphotungstic acid hematoxylin,  $\times 15$ , B, connective tissue stroma in tumor implant, Perdraus stain,  $\times 620$

other gliomas by the presence of "Basalkörperchen" or "Blepharoplasten" in the cells of the former. These basal bodies do not occur in any other tumors of the nervous system except pinealomas. The same method therefore serves as an advantageous means of distinguishing papillomas of the choroid plexus from papillary ependymal tumors.

<sup>1</sup> Mallory, F. P. Three Gliomas of Ependymal Origin. *J. M. Research* 3:1, 1902.

and has been so employed by Saxer, Bielschowsky and Unger, Sjovalf, Davis and Cushing, and others. Another equally valuable means of distinguishing papillomas of the choroid plexus is by the connective tissue framework. Whether this is abundant or scanty, it can be distinguished by suitable means, such as the connective tissue stain of Perdrau or van Gieson, from the glial structure forming the framework of ependymomas. Then too the epithelium of plexus tumors abounds in coarse granular often conglomerate mitochondria compared with the scanty minute mitochondrial bodies of ependymomas.



Fig. 11 (case 2) —Papilloma of the choroid plexus showing the architecture of the tumor and the connective tissue stroma, Perdrau's connective tissue stain,  $\times 150$

It has generally been considered that plexus tumors are not "seeded" by the cerebrospinal fluid, while it is not an infrequent occurrence in

2 Saxer, F. Ependymepithel Glome und epitheliale Geschwülste des Centralnervens systems. *Zeiglers Beitr. z. path. Anat.* **32**: 276, 1902.

3 Bielschowsky, Max, and Unger, Ernst. Zur Kenntnis der primären Epithelgeschwülste der Adergeflechte des Gehirns. *Arch. f. klin. Chir.* **81**: 61, 1902.

4 Sjovalf, Einar. Ueber eine Ependymcyste embryonalen charakters (Paraphyse?) im dritten Hirnventrikel mit tödlichen Ausgang. *Beitr. z. path. Anat. u. z. allg. Pathol.* **47**: 248, 1909.

5 Davis, L. E. and Cushing, Harvey. Papillomas of the Choroid Plexus with a Report of Six Cases. *Arch. Neurol. & Psychiat.* **13**: 681 (June) 1925.

ependymal tumors. However, there would seem to be considerable evidence that this manner of spread does occur. LeBlanc,<sup>6</sup> in 1868, reported a tumor of the left lateral ventricle "the size of child's fist," with two small well delimited implants in the subpial tissues of the right cortex. All were of identical macroscopic appearance. From the sketch there can be little doubt but that the growth was a papilloma of the choroid plexus (fig 12). Bielschowsky and Unger<sup>7</sup> also reported a tumor which arose in the region of the right flocculus of the cerebellum, with about fourteen implants over the surface of the cortex, all were identical with the original tumor. From the description and illustrations it would seem reasonably certain that they are derived from



Fig 12 (case of LeBlanc)—Papilloma of the left lateral ventricle (From Beitr z path Anat d Gehirn Tumoren, Inaug Dissert, Bonn, 1868)

a papilloma of the choroid plexus of the fourth ventricle. Von Bouwdijk<sup>7</sup> has recorded a probable though not certain case which is also an example of this (fig 20). There was a cystic tumor of the cerebellum, with seeding of countless tumors in the subarachnoid spaces. The tumor structure of the original growth was a papillomatous one made up of cores of connective tissue covered with high columnar non-ciliated epithelium. The smaller tumors were all of a similar nature. Autopsy did not reveal any other tumor in the body from which

6 LeBlanc, Christian. Papillom Maxillotodes, Beitr z path Anat d Gehirn Tumoren. Inaug. Dissert. Bonn, 1868.

7 Von Bouwdijk, Bastiaan. Primäres metastasierender Gehirne carcinom, Ztschr f d Ges Neurol u Psychiat 27:96, 1914.

metastases could have occurred. It is hardly conceivable that the original tumor was a hidden carcinoma metastasizing to subarachnoid spaces alone. Neither does the tumor appear to be an instance of "sarcomatosis of the leptomeninges" recently reviewed by Bailey.<sup>8</sup> The case of Bencke<sup>9</sup> may possibly be another example. Toppich<sup>10</sup> has described a papillomatous tumor of the choroid plexus of the fourth ventricle with numerous seedings in the subarachnoid space over the cerebrum and cerebellum and also about the spinal cord. He considered that the original tumor was carcinomatous because of invasion of the cerebellum. Such a phenomenon as this, however, is not conclusive evidence of true

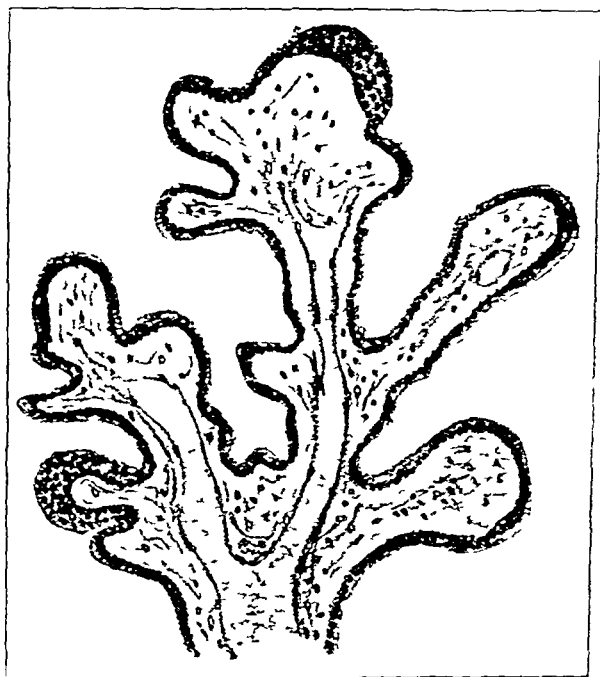


Fig. 13 (case of Ribberts).—Papilloma of the fourth ventricle. (From *Geschwulstlehre* 1904.)

malignancy, and has been observed by Cushing and others. Pushing of papillae of the tumor between the leaflets of the cerebellar cortex is to be more truly looked on as the direct result of pressure. Gromelski.<sup>11</sup>

8 Bailey, Percival. Intracranial Sarcomatous Tumors of Leptomeningeal Origin. *Arch. Surg.* **18** 1359 (April) 1929.

9 Beneke, R. Casuistische Beiträge zur Geschwulstlehre. *Virchows Arch. f. path. Anat.* **119** 60 1890.

10 Toppich, G. Die Zottenkrebs-e des Adergeflechtes der Rautengrube. *Frankfurt Ztschr. f. Path.* **33** 238 1925.

11 Gromelski, Alfred. Beitrag zu der Lehre von den primären epithelialen Geschwulsten des Zentralnervensystems. *Virchows Arch. f. path. Anat.* **261** 933 1926.

reported a curious papillary epithelial tumor with a connective tissue core found in the lumbar region of the spinal canal. His description of the brain was not adequate to show whether this had its origin from a tumor of the choroid plexus by seeding or whether it arose from an embryologic rest as the author assumed.

In case 2 here reported, the left temporal horn is studded with hundreds of minute tumors which are identical macroscopically and



Fig 14 (case of Bielschowsky and Unger) —Papilloma of the fourth ventricle (From *Arch f klin Chr* 81 61, 1905)

microscopically with the original tumor and which are quite apart from it. The implant in the dilated right lateral ventricle is well away from the original growth and represents a true tumor implantation, both macroscopically and microscopically (fig 9). The smaller nodules are epithelial only in character, while the larger lateral ventricle transplant has a scanty connective tissue core (fig 10A). Seeding of tumors through the cerebrospinal fluid spaces cannot be looked on as evidence

of malignancy of the tumor but is probably an accidental occurrence in which trauma may well play a considerable part

Tumors of the choroid plexus of the lateral ventricle are particularly apt to have an enveloping membrane about them. This membrane may be closely applied to the surface of the tumor as in case 1 or separated from it by fluid which has been poured out by the tumor cells. Occasionally this process goes on to such an extent that it leaves the tumor



Fig 15—Section of papilloma shown in figure 14

like a nodule in a cyst wall. A few such blood vessel tumors undoubtedly tend to be self-destructive in this manner.

Another distinguishing feature of plexus tumors is their benign nature and lack of invasive tendencies. Papillae occasionally push their way for a short distance into brain substance in which softening from contiguous pressure has occurred or between leaflets of the cerebellar cortex.

There are in the literature a few reports of papillary tumors of the choroid plexus which because of their invasive tendencies merit the term carcinoma. The most notable examples are the cases of Rokitan-





Fig 16 (case of Rheindorf) —Tumor of the fourth ventricle (From Charité Ann 32 294 1908)

sky, Spaet<sup>12</sup>, Korner<sup>14</sup> (case 1) and Kolpin<sup>15</sup>. The most adequately described and illustrated case of eucarcinoma of the choroid plexus in the literature is that of Lehoczký<sup>16</sup>. The case of Esser<sup>17</sup> seems very doubtful and is more likely a benign papilloma of the plexus that is pushed into adjoining tissue space.

*Cysts of the Choroid Plexus*—In going over the literature on the tumors of the choroid plexus i.e. papillomas, eucarcinomas, endotheliomas, lipomas, sarcomas, chondromas, etc. one is struck with the fact that the great majority of cysts are associated with the papillomas. In the main they tend to occur where epithelial growth has outstripped its blood supply. With the exception of one type the cysts seem to have been formed primarily at the expense of the connective tissue and vestiges of epithelium can be found covering the cyst wall or near its base. Sjoval<sup>18</sup> reported a case in which the cyst was connected with



Fig 17 (case of Boudet and Clunet) —Papilloma of the right lateral ventricle (From Arch de med exper et d'anat path 22 379, 1910)

the choroid plexus of the third ventricle and lined with epithelium of an embryonic ependymal ciliated nature. Typical blepharoplasten were found in the cells.

Calcification, as noted in case 2, represents deposits of lime salt in old hemorrhagic areas and not about blood vessels as described by van Dessel in gliomas of the brain. My case 2, the case of Robin and

12 Rokitsky, Carl. Lehrbuch d path Anat 3 1856 vol 2, p 425

13 Spaet, Primärer Multipler Epithelkrebs des Gehirns, Aertzi Intelligenzbl 30 305, 1883

14 Korner, Hildegard. Geschwülste der Adergeflechte, Zentralbl f allg Pathol u path Anat 30 121, 1919

15 Kolpin. Multiple Papillome (Adeno-Carcinome) des Gehirns. Arch f Psychiat 45 595, 1909

16 Lehoczký, T. Zur Frage der Primären Gehirn carcinome. Arch f Psychiat 82 527, 1928

17 Esser, A. Ein Carcinom des Plexus chorioideus des IV Ventrikels. Ztschr f d ges Neurol u Psychiat 106 511, 1906

Blondel<sup>18</sup> and that of Luttgen<sup>19</sup> seem to be the only instances in which calcification has been reported in this type of tumor

The most common location for these tumors is in the fourth ventricle, the second in the lateral ventricles and the least common in the third ventricle. Of the forty-seven cases here assembled twenty-three were in the fourth ventricle, seventeen in the lateral ventricles and six in the third ventricles. It is a curious coincidence that of all the reported papillomas of the lateral ventricles 93 per cent are of the left side.

Cushing's series of verified tumors furnishes about the only available information as to incidence. He reports six true cases among 964 verified tumors, or 0.6 per cent.

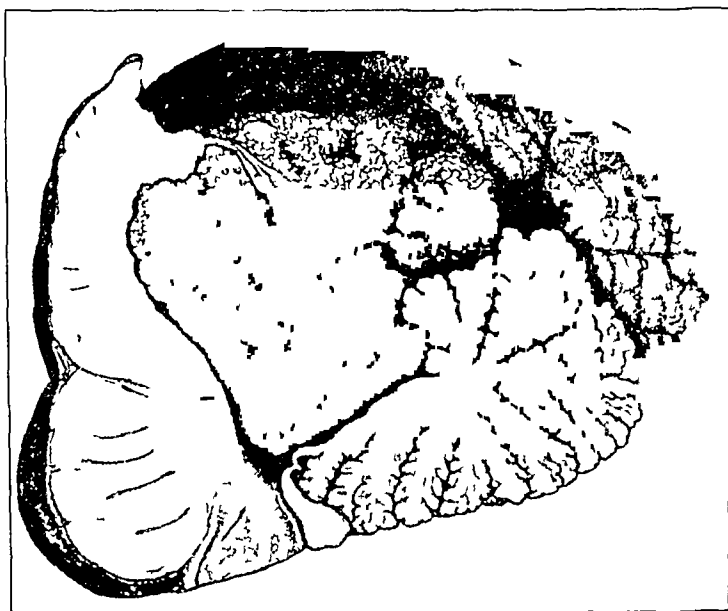


Fig. 18 (case of Vonwiller)—Papilloma of the fourth ventricle (From Virchows Arch f. path. Anat. **204**: 230, 1911.)

Simple symmetrical or regional hypertrophy of the choroid plexus does occur. A notable example is that reported by Cushing. Hydrocephalus was assumed to have arisen from an increased production of fluid. The question as to where simple hypertrophy ends and papillomatous tumor formation begins is an academic one. The case reported by von

<sup>18</sup> Robin and Blondel. Description d'une tumeur épithélioïde provenant du plexus choroïde dont elle garde la structure fondamentale. *Gr. méd. de Paris* **32**: 7 and 506, 1858.

<sup>19</sup> Luttgen, Paul. Ueber ein Fall von Papillom des Plexus chorioideus. *Inaug. Dissert.* Würzburg, 1896.

Plath<sup>20</sup> is that of a local hypertrophy of the choroid plexus, with hydrocephalus presumably from excessive formation of fluid

The age incidence for these tumors is a gradually diminishing one In thirty-five cases in which the age is given, there were nine cases in the first decade, seven in the second five in the third, four in the fourth five in the fifth and three in the sixth

#### SURGICAL EXPERIENCES

The first surgical attempt made toward removal of one of these tumors is reported in the case of Bielschowsky and Unger The cases



Fig 19 (case of Natonek)—Papilloma of the fourth ventricle (From Virchow's Arch f path Anat **218** 170, 1914-)

in which operative procedures have been undertaken are listed as follows

Observer	No of Cases	Outcome
Bielschowsky and Unger	One	Fatality
Bowditch	One	Fatality
Perthes	One	Recovery
Sachs	One	Recovery
Cushing	Two	Fatality
	One	Patient lived for 3 months
	Two	Patients were living and well 1 year later
	One	Patient was living and well 18 months later
Van Wagenen	One	Patient was living and well 5 months later

<sup>20</sup> Von Plath Hyperplasie der plexus choroideus laterales bei hydrocephalus internus congenitus Jahrb f Kinderh **21** 417 1884

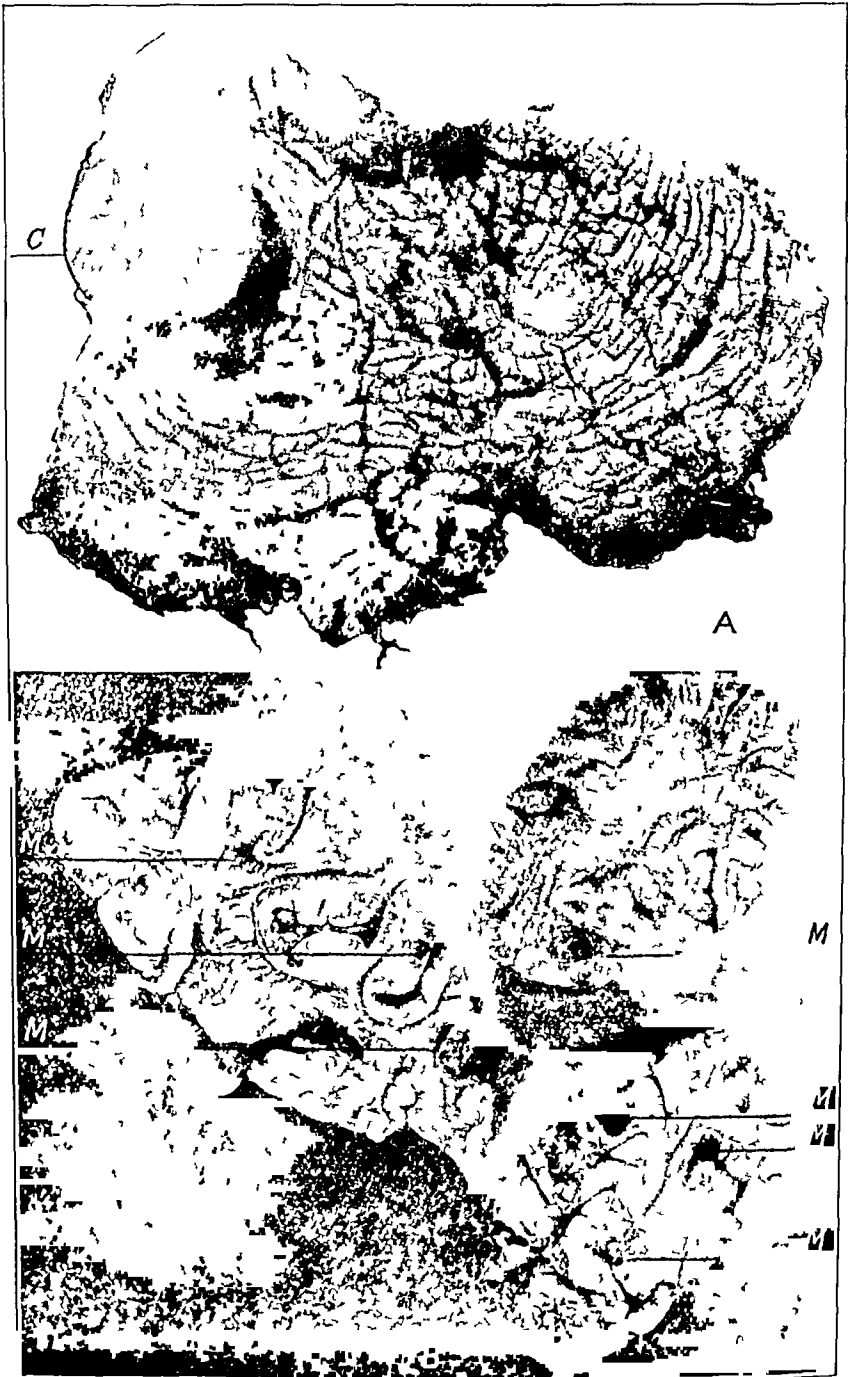


Fig 20 (case of Bouwidijs) —*A*, cystic tumor of the cerebellum, *B*, sites of subarachnoid tumor transplants (From *Ztschr f d ges Neurol u Psychiat* 27 96, 1914)

CASES REPORTED IN THE LITERATURE

CASE 1 (Guerard<sup>21</sup>)—In a patient, aged 3, autopsy revealed a tumor of the posterior end of the right lateral ventricle the size of a hen's egg which was lobulated and enclosed in a thin membrane. The tumor was in contact with the choroid plexus, was granular on section, very vascular, and made up of small blood vessels and epithelial elements.

CASE 2 (Robin and Blondel<sup>22</sup>)—In a patient, aged 11, a tumor, 6 by 4 by 3 cm was found lying free in the fourth ventricle. The tumor was made up of papillary-like growths closely resembling the normal structure of the choroid plexus and replacing the normal plexus structure. One or more layers of epithelium were found covering the papillae. Calcareous particles were found occasionally.

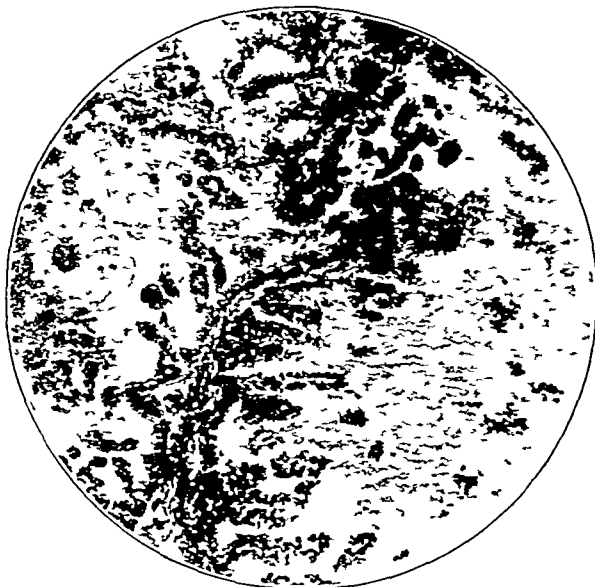


Fig 21 (case of Bouwidijsk)—Microscopic section of tumor making up part of wall of cyst. (From *Ztschr f d ges Neurol u Psychiat* 27 96, 1914.)

CASE 3 (Levrat-Perroton<sup>23</sup>)—In a patient aged 25 a fourth ventricle tumor the size of a nut was attached to the choroid plexus from which it arose. The tumor compressed the cerebellum but was separated from it, penetrated the aqueduct of Sylvius and separated the cerebral peduncles. It was gelatinous, transparent, of colloid consistency and covered by epithelial cells. The center of the tumor was made up of amorphous material with connective tissue strands bearing blood vessels subdividing it here and there.

CASE 4 (LeBlanc<sup>24</sup> case 1)—In a patient aged 60 an original tumor the size of a child's fist was found on the floor of the left lateral ventricle. Two small tumors the size of a pea-seed were also found partly buried in the tissues of the surface of the right cortex but in connection with the subarachnoid space. These

21 Guerard. Tumeur tongueuse dans le ventricule droit du cerveau chez une petite fille de trois ans. *Bull Soc anat de Paris* 8 211 1832-1833.

22 Levrat-Perroton Francois. Thèse de Paris 1899.

nodules lay at the entrance of the small vessels of the pia into the cortex of the brain. Macroscopically and microscopically all these tumors were alike. The large tumor was made of a central core of blood vessels which branched out into delicate papillae. The papillae were covered with cylindric epithelium. There were no cilia (fig 12).

CASE 5 (Kelly<sup>23</sup>)—In a patient, aged 11, autopsy disclosed a tumor of the fourth ventricle, 1 by 1½ inches (2.5 by 3.8 cm) in size, which distended the ventricle and appeared at the base at the left of the medulla. The tumor had a granular surface, was irregular in shape, yellowish red, and was made up of a vast number of delicate villous tufts, each equipped with a thin-walled vessel and

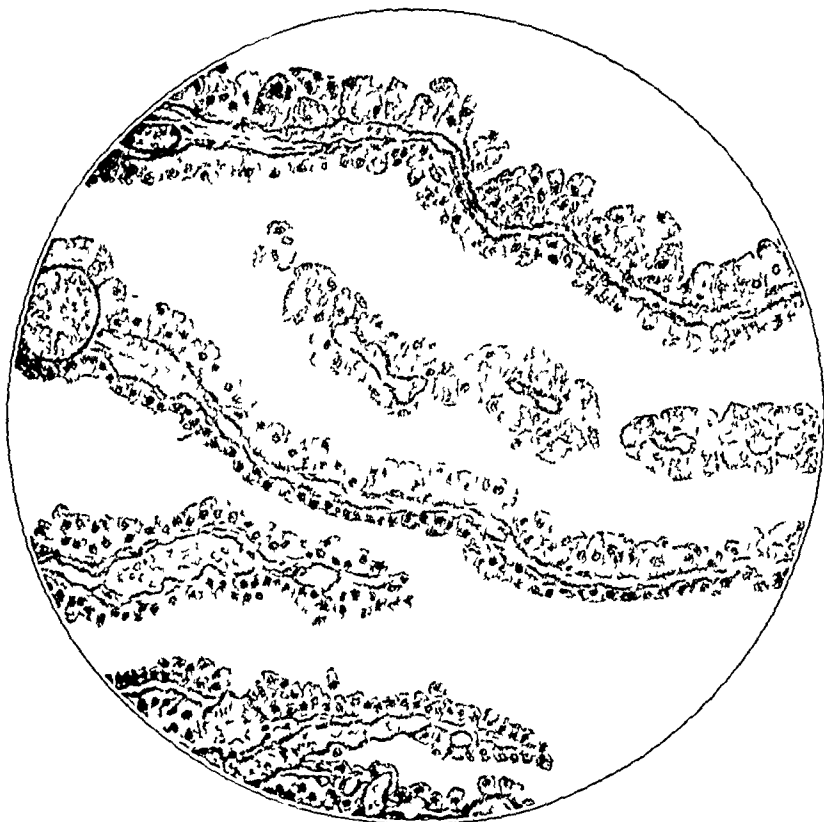


Fig 22 (case 2 of Korner)—Papilloma of the right lateral ventricle. (From *Centralblatt für allg Pathol u path Anat* 30:121, 1919.)

covered with columnar epithelium. "It seemed to have grown from the choroid plexus" (This case has come down in the literature as that of Dr. Garrod under whose hospital care the patient was.)

CASE 6 (Chouppé<sup>24</sup>)—In a patient, aged 42, a tumor of the fourth ventricle arising from the choroid plexus and compressing the cerebellum was uncovered at autopsy. The tumor consisted of a light connective tissue framework bearing large capillaries and covered with epithelium.

23 Kelly, Charles. Papilloma of the Fourth Ventricle, *Tr Path Soc London* 24:6, 1873.

24 Chouppé. Etude sur les tumeurs du quatrième ventricule, Verron, Thèse de Paris, 1873.

CASE 7 (Demange<sup>25</sup>)—A tumor the size of a nut was found in the left lateral ventricle of a patient aged 8. It was pedunculated and attached to the choroid plexus and formed by a heaping up of the choroid plexus. There was an accompanying chronic hydrocephalus.

CASE 8 (von Plath<sup>26</sup>)—The patient, aged 3, was considered to have died of congenital hydrocephalus. The ependyma of the ventricles was smooth and



Fig 23 (case of Priesel)—Papilloma of the fourth ventricle (From Virchow's Arch f path Anat **253** 125 1924)

glistening. The choroid plexus of both ventricles was very thin from the foramen of Monro to the beginning of the posterior horn where it thickened out on both sides to the size of a walnut and then tapered off again. The author con-

25 Demange E. Paraplegia incomplete, scarlatine, albuminurie, symptoms d'urémie. Autopsie, hydrocephale ventriculaire. Bull Soc anat de Paris **49** 503 1924.



sidered that overproduction of cerebrospinal fluid by the tumorous plexuses might have been the cause of the hydrocephalus

CASE 9 (Audry,<sup>6</sup> case 1) —Autopsy on a patient, aged 45, disclosed a tumor of the left ventricle the size of a small nut. The tumor was spongy, friable, attached to the choroid plexus, covered with a fibrous capsule and made up of connective tissue and blood vessels. The cells resting on the blood vessels were granular, with round or oval nuclei.

CASE 10 (Douty<sup>2</sup>) —In a patient aged 17, autopsy revealed a large tumor, the size of a bantam's egg, free in the fourth ventricle. It was attached to the roof of the ventricle by two delicate strands of membranous connective tissue conveying blood vessels. The tumor was mulberry-like, friable, gelatinous, non-invasive, villous and "agrees in structure with the fringes of the choroid plexuses of the ventricles."

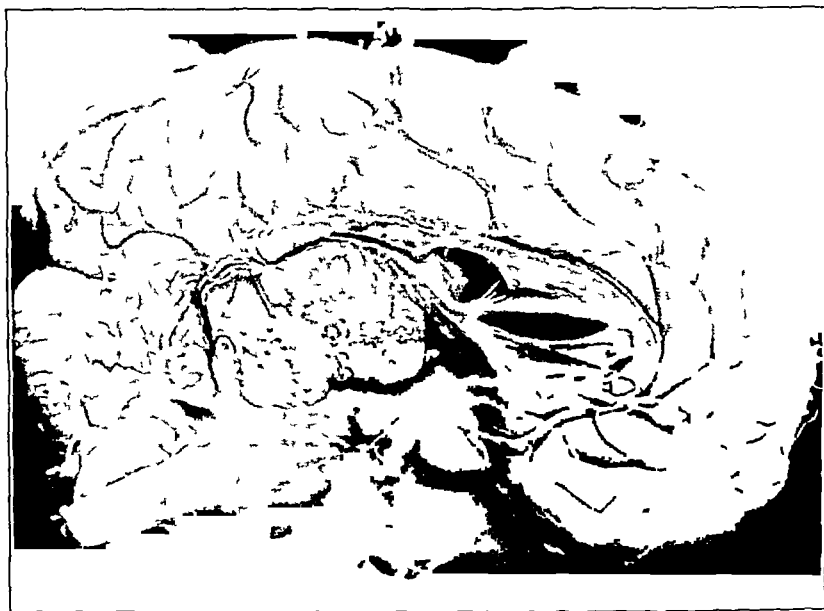


Fig. 24 (case of Noodt) —Papilloma of the third ventricle. (From Virchows Arch f path Anat **258** 331, 1925)

CASE 11 (Beneke,<sup>9</sup> case 2) —In a patient aged 26, a tumor of the third ventricle was found at the entrance of the infundibulum. It was grayish red, soft, mulberry-like and rather loose from the ependyma which was everywhere lightly granular. The pineal gland was normal.

In the cavity of the fourth ventricle lay a tumor, 4 by 2 by 2.5 cm, which compressed the pons and medulla and was connected with the brain stem only by loose tissue filaments. The cerebellum was more firmly connected with the tumor in the region of the anterior vermis. "Microscopically the tumor is a typical papilloma whose short, knitted, filamentous forms have a relationship with the embryonal growth formations of ependymal filaments, for example the choroid plexus."

26. Audry, J. Les tumeurs des plexus choroïdes, *Rev. de med.* **11** 897, 1886.

27. Douty, J. Harrison. Notes and Remarks upon a Case of Villous Tumor in the Fourth Ventricle, *Brain* **8** 409 1885-1886.

CASE 12 (Stroeber<sup>28</sup> case *b*)—Autopsy on a patient, aged 1 year and 6 months, revealed a tumor of the left ventricle the size of a walnut. Tumor also filled the temporal horn but did not invade brain substance. Microscopically the appearance was that of the choroid plexus.

CASE 13 (Hess<sup>29</sup>)—In a patient aged 31, a tumor composed of two parts was found in the fourth ventricle at autopsy, the smaller part measured 1 by 1.5 cm, and the larger 1.5 by 2.5 cm. The tumor was cauliflower-like and reddish gray, it compressed the pons medulla and cerebellum but did not invade it. Microscopically it proved to be a papillary growth made up of blood vessel cores covered with epithelial cells.

CASE 14 (Luttgen<sup>30</sup>)—A tumor of the third ventricle, the size of a pigeon's egg, was found at autopsy. The tumor was connected with the choroid plexus



Fig. 25 (case of Noodt)—Papilloma of the left lateral ventricle. (From Virchows Arch f path Anat 258 331, 1925.)

and was made up of papillae of varying sizes and breadths. The papillae were covered with cylindrical epithelium. There were calcareous concretions in the tumor.

CASE 15 (Auvray<sup>30</sup>)—A tumor of the fourth ventricle was found which was about 4 by 5 cm in size and of the form of a large chestnut. Microscopically it was made up of well filled capillaries with immature endothelium and a loose structure of round and even cells set together which appeared like a growth of plexus epithelium.

28 Stroeber H. Papillom des Plexus chorioideus im linken Seitenventrikel. Berl klin Wehnschr 30 123 1893.

29 Hess Friedrich. Beiträge zur Geschwulstlehre. Inaug. Dissert. Bonn 1896.

30 Auvray. Tumor des plexus chorioideus des Fourth Ventracles. Centrallbl allg Pathol u path Anat 9 275 1898.

CASE 16 (Bruchanow<sup>31</sup>) —In the left "cella media" there was found a tumor, 5 cm in diameter, which was connected with the choroid plexus. It showed an exquisite papillary structure. The whole tumor resembled a normal choroid plexus. The epithelium was low cylindric.

CASE 17 (Henneberg<sup>3</sup>) —A walnut-sized, hard, uneven tumor was found at autopsy in connection with the choroid plexus of the third ventricle. The distal end of the tumor reached through the iter into the fourth ventricle. The tumor showed a papillary structure. The epithelium about the connective tissue structures bearing the blood vessel was high cuboidal.

CASE 18 (Ribberts<sup>32</sup>) —A tumor of the fourth ventricle was found. Figure 13 shows it to be typical of a choroidal plexus papilloma.

CASE 19 (Bielschowsky and Unger<sup>3</sup>) —Autopsy on a patient, aged 43, showed a tumor arising in the region of the right flocculus of the cerebellum with about fourteen identical smaller tumors scattered over the surface of both hemispheres. The symptoms produced by one of these tumors over the left cortex led to a craniotomy at which time a portion of the tumor was removed. Reoperation at the same site three months later proved fatal.

All of the tumors were sharply separated from the surrounding brain and all were in direct connection with the subarachnoid space, with one possible exception. This one subcortical tumor lay along a blood vessel dipping down into the brain, and the tumor arose on the blood vessel as if on a pedicle. There were also two small tumors found at the base in the region of the sixth nerves.

Microscopically the tumor proved to be composed of epithelium which rested on blood vessels and was arranged radially about the lumen of the vessel (fig 14).

Comment. This would seem to be a probable example of a papilloma of the plexus of the fourth ventricle which spread by "seeding" in the cerebrospinal fluid system.

CASE 20 (Vigouroux<sup>31</sup>) —At autopsy the fourth ventricle was found filled with a tumor the size of a nut, arising from the choroid plexus. All the ventricles were dilated.

CASE 21 (Rheindorf<sup>35</sup>) —Tumor of the fourth ventricle, 4 by 2.5 cm, with a true papillary structure and connected with the choroid plexus (fig 16) was found in a patient aged 21.

CASE 22 (Slavmaker and Elias<sup>36</sup>) —A tumor of the fourth ventricle, 4.2 by 4 by 5.2 cm, was found at autopsy in a patient aged 11. It filled the entire ventricle and projected downward between the cerebellum and the medulla. The tumor was directly continuous with the choroid plexus which appeared to be

31 Bruchanow, N. Ueber einen Fall von Papillom des Plexus chorioideus ventriculi lateralis sinister bei einem 2½ jährigen Knaben, Prag med Wchnschr **23** 585, 1898.

32 Henneberg. Ueber einen Fall von Papillärer Geschwulst des Plexus chorioideus in dritten ventricle, Berl klin Wchnschr **12** 277 1903.

33 Ribberts, Hugo. Geschwulstlehre, Bonn, Friedrich Cohen, 1904, p 359.

34 Vigouroux, A. Écoulement de liquide céphalo-rachidien hydrocéphalie papillome des plexus choroïdes du quatrième ventricle, Rev neurol **26** 281, 1908.

35 Rheindorf. Papilläres Epithelom des vierte Ventricules, Charité-Ann **32** 294 1908.

36 Slavmaker, S. R. and Elias, F. Papilloma of Choroid Plexus with Hydrocephalus Arch Int Med **3** 289 (May) 1909, Chicago Path Soc **7** 187, 1907-1909.

larger than normal. Microscopically there were "slender stalk-shaped villous branching and greatly tangled frameworks of connective tissue covered with columnar epithelium arranged for the most part in a single layer."

CASE 23 (Boudet and Clunet,<sup>37</sup> case 1) —At autopsy on a patient, aged 45, there was found a tumor, 3 or 4 cm. in size, situated in brain substance but continuous with the choroid plexus on the right side. The lateral ventricle was obliterated and the tumor curved downward into the temporal horn of the ventricle. The tumor consisted of two parts: an internal cystic and cavernous portion and a covering papillomatous portion. The papillae of the latter were formed by vascular connective tissue covered with cuboidal epithelium which reproduced the structure of the normal plexus. The tumor had invaded the nerve tissue in places, and deep in the brain were strands of epithelial cells which probably represented a pushing out of papillae into softened brain substance (fig. 17).

CASE 24 (Vonwiller<sup>38</sup>) —A tumor, 3.5 by 3 cm., lying free in the fourth ventricle and not invading any of the surrounding structures was found at autopsy on a patient aged 15½ years. The tumor arose by a pedicle from the region of the obex. It was a papillary growth made up of a stroma of blood vessels and connective tissue which was covered by epithelium. The whole structure was considered to resemble closely normal choroid plexus. No cilia were found on the epithelium (fig. 18).

CASE 25 (Natonek<sup>39</sup>) —A walnut-sized tumor filling the fourth ventricle and lateral recesses was found at the medial side of the flocculus. Microscopic examination showed a tumor with many long and some short filamentous processes. The epithelium covering the filaments was in single rows for the most part. Most but not all of the papillae had a central blood vessel (fig. 19).

CASE 26 (von Bouwduyk<sup>40</sup>) —In a patient aged 57, symptoms referable to a tumor of the cerebellum had led to an operation being performed in that region. A solid papillomatous tumor was removed. Death occurred a few hours later. At autopsy another tumor of the posterior fossa was found which was circumscribed, nut-sized and gelatinous, with an uneven surface. The tumor rested on the surface of the cerebellum, stood out from it somewhat and was but little connected with its surrounding tissues. Grossly, no other nodules were noted in the cerebellum. After fixation in a diluted solution of formaldehyde, a number of tiny nodules were seen in the subarachnoid spaces over both hemispheres. All rested superficially and in connection with the subarachnoid space. Almost all were single, gelatinous, rather hard and whitish gray. There were none in the gray matter or the basal ganglia. In a careful autopsy no source for a primary tumor was found elsewhere. The larger tumor in the cerebellum was a cystic one which raised itself above the surface of the brain. When the cyst was opened a papillary tumor was found to make up a part of its inner wall.

Microscopic examination showed the cyst wall of the primary tumor to be made up of a covering of connective tissue which was poor in cells. The solid

37 Boudet C. and Clunet S. Contribution à l'étude des tumeurs épithéliales primitives de l'encéphale développées aux dépens des formations dépendantes et particulièrement des plexus choroïdes. Arch. de méd. exper. et anat. path. **22**: 379, 1910.

38 Vonwiller Paul. Ueber das Epithel und die Geschwülste der Hirnkammern. Virchows Arch. i. path. Anat. **204**: 230, 1911.

39 Natonek Desider. Zur Kenntnis der primären epithelialen Tumoren des Gehirns. Virchows Arch. i. path. Anat. **218**: 170, 1914.

nodule in the cyst wall was composed of papillae with a connective tissue stroma rich in blood vessels. The papillae were covered by a layer of high cylindrical epithelium. Nowhere were cilia to be seen. No glia fibers were found.

The metastases were in part cystic. Microscopically they proved to have the same papillary structure as the tumor described (fig 20 B).

CASE 27 (Weygandt<sup>40</sup>)—Autopsy on a patient, aged 10 months, revealed a tumor of the left ventricle, 7.3 by 8 cm. in size, which showed a papillary structure and which was definitely connected with the choroid plexus. Microscopically the cells had an outspoken epithelial character with giant cells here and there containing 2 or 3 nuclei. The blood vessels were abundant and thin-walled, with hemorrhages into the tumor.

CASE 28 (Goodhard<sup>41</sup>)—In a patient, aged 6 months, a tumor of the right lateral ventricle, 4 by 3.5 by 3.5 cm., attached to the choroid plexus was found at autopsy. It was firm and reddish purple, and nowhere did it invade the brain. It was composed of a number of papillomatous processes containing a central capillary and covered with a single layer of short columnar epithelium. There was a hydrocephalus of all ventricles considered by the author to be due to an excessive formation of fluid.

CASE 29 (Korner<sup>42</sup>)—Autopsy on a patient aged 9 revealed a tumor, 8.5 by 5 cm. in size, in the right lateral ventricle. Microscopically it was a typical papilloma of the choroid plexus (fig 22).

CASE 30 (Perthes<sup>43</sup>)—In a patient aged 47, a large left-sided tumor arising from the choroid plexus and extending to the surface of the brain in the occipital region was surgically extirpated. The tumor showed a papillary structure and was partly cystic. The papillae were made up of blood vessels covered with large epithelial cells.

CASE 31 (Lorenzini<sup>44</sup>)—In a patient aged 10 years, a tumor the size of a hen's egg was found in the third ventricle extending from the anterior pillars of the trigone to the posterior white commissure. It was connected at its base with the choroid plexus. The tumor was partly cystic and filled with yellowish fluid as were also the lateral ventricles. The external surface of the tumor was irregular and nodular. The solid portion of the tumor had a papillary structure made up of epithelial cells in one or more layers. There were numerous small cysts in the solid portion of the tumor. It was everywhere sharply demarcated from nerve tissue.

CASE 32 (Sachs<sup>45</sup>)—In a patient aged 55, a well encapsulated tumor which filled the fourth ventricle and extended into the aqueduct of Sylvius was surgically extirpated. A microscopic study did not accompany the report, but Cushing reports that a later examination proved the tumor to be a true papilloma of the choroid plexus.

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40 Weygandt. Hydrocephalus mit Tumor (Papillom des Plexus chorioideus), *Deutsche med. Wchnschr.* **43** 797, 1917.

41 Goodhard, G. W. Adenoma of the Choroid Plexus, *Guy's Hosp. Rep.* **69** 217, 1918.

42 Perthes. Glückliche Entfernung eines Tumors des Plexus chorioideus aus dem Seitenventrikel des Cerebrum. *München med. Wchnschr.* **66** 677, 1919.

43 Lorenzini. Aldo. Papilloma cistico del terzo ventricolo, *Riv. di clin. pediat.* **20** 705, 1922.

44 Sachs. Ernest. Papilloma of the Fourth Ventricle. Report of a Case, *Arch. Neurol. & Psychiat.* **8** 379 (Oct.) 1922.

CASE 33 (Priesel<sup>45</sup>)—A chance observation at autopsy on a patient, aged 74, was a tumor of the fourth ventricle, 15 by 12 by 1 cm in size that was definitely connected with the choroid plexus. Vessels could be seen entering the tumor from the plexus. It arose from the region of the calamus scriptorius. Microscopic examination showed it to be composed of many broad papillae with a fine framework of blood vessels bearing connective tissue. Cuboidal and columnar epithelium covered the papillae. Many of the epithelial cells contained pigment (fig 23).

CASE 34 (Okabe<sup>46</sup>)—At autopsy on a patient aged 5 months, a tumor of the third ventricle was found arising from the choroid plexus. The tumor extended into the lateral ventricles. A microscopic report is not given.

CASE 35 (Noodt<sup>47</sup> case 1)—Autopsy on a patient, aged 33, revealed a tumor 5 by 3 cm occupying the third and lateral ventricles and the aqueduct of Sylvius. It bordered anteriorly on the septum pellucidum and the fornix, above on the corpus callosum and behind on the splenium, the recessus pinealis and the stria medullaris, the posterior commissure, and underneath on the thalamus. A small part of the tumor lies in the sylvian aqueduct. The growth was cystic in its posterior portion. Microscopically the stroma was made up of connective tissue which was rich in blood vessels but poor in cellular elements. The papillae of the tumor were covered in part with a single-layered, high, nonciliated, cylindric epithelium in part with a cuboidal epithelium of more than one layer. The picture was that of "a papillary epithelioma of the choroid plexus." It was not, the author said, of pineal gland origin (fig 24).

CASE 36 (Noodt<sup>47</sup> case 2)—An irregular lobulated tumor of the left lateral ventricle 6 by 4 by 4 cm, was found at autopsy on a patient aged 1. The tumor was made up of very small papillae rich in blood vessels and containing little connective tissue stroma. The papillae were covered with a high, single-layered cylindric epithelium (fig 25).

CASE 37 (Davis and Cushing case 1)—In a patient aged 22, a tumor of the fourth ventricle, approximately 5.5 cm in diameter, was removed through an incision in the left cerebellar hemisphere. Microscopically the tumor "showed a papillomatous structure comprised of numerous cauliflower-like villi, which had a central core of loose fibrous connective tissue. The epithelial cells covering the villi were cuboidal in shape and were arranged in one layer. The cells did not contain blepharoplasts and glia fibers were not present."

CASE 38 (Davis and Cushing case 2)—Autopsy on a patient, aged 9, revealed a tumor of the left lateral ventricle surrounded by a number of smooth lined cysts. The villi were arranged in a somewhat compact fashion and only in places showed typical papillomatous characteristics. They consisted of a very small central core of loose white connective tissue, in which were situated blood vessels. Each villus was clothed by a single layer of cuboidal cells.

CASE 39 (Davis and Cushing case 3)—At operation on a patient aged 50 a fragment of tumor was removed for microscopic study. It proved to be a part of a papillomatous growth. The villi were long and narrow and exhibited many side branches. Blepharoplasts and glia fibers were absent. The tumor was in the left hemisphere.

45 Priesel A. Ein Beitrag zur Kenntnis der Tumoren der Plexus Chorioidei. Virchows Arch u path Anat **253** 125 1924.

46 Okabe Yotsu. A Case of Papilloma of the Plexus Chorioideus in a Child. Gann **18** 28 1924.

47 Noodt Klara. Ein Beitrag zur Kenntnis der Papillären Epitheliome des Plexus chorioideus. Virchows Arch u path Anat **258** 351 1925.

CASE 40 (Davis and Cushing,<sup>5</sup> case 4) —At operation on a patient, aged 30, a fragment of tumor was removed from an incision in the right cerebellar hemisphere. On microscopic examination it showed "numerous villi which were somewhat larger than normal and much more numerous. They had a characteristic cauliflower appearance. The central core of each villus consisted of loose white fibrous connective tissue containing numerous blood vessels. The epithelial cells covering these villi were cuboidal in shape and arranged in a single layer."

CASE 41 (Davis and Cushing,<sup>5</sup> case 5) —A portion of a very vascular tumor was removed from an incision through the vermis of the cerebellum in a patient aged 27. "It had the characteristic papillomatous structure which identified it as having originated from the choroid plexus. The villi were numerous, long, wide and possessed many side branches. The central core consisted of a dense, white, fibrous connective tissue with blood vessels. The epithelial cells were cuboidal in shape, and the cytoplasm was finely granular."

CASE 42 (Davis and Cushing,<sup>5</sup> case 6) —In a patient aged 28, a tumor, approximately 4.5 cm in diameter, was surgically removed through an incision in the vermis of the cerebellum. "Microscopically sections revealed the typical papillomatous appearance, with villi much larger than those encountered in a normal choroid plexus. The central core contained very little white fibrous tissue, being made up for the most part of loose reticular tissue. There were numerous blood vessels with very thin walls. The epithelial cells were tall and columnar with oval or cylindrical centrally placed nuclei."

CASE 43 (Toppich<sup>40</sup>) —Autopsy on a patient, aged 2, revealed a tumor completely filling the fourth ventricle. There were also numerous secondary nodules in the subarachnoid spaces of the basilar systems, about the cerebellum and in the lower part of the spinal canal. The tumor arising from the choroid plexus was composed of a papillae made up of epithelial cells, mostly high columnar, resting on a connective tissue framework. Blood vessels were abundant in the connective tissue spaces. The original tumor had pushed its way into the cerebellum near the fastigium.

CASE 44 (Zalka<sup>48</sup>) —A tumor of the fourth ventricle compressing pons and medulla and cerebellum was found at autopsy. It was made up of blood vessels and connective tissue arranged in papillary form covered with cylindric epithelium. The structure was considered to be typical of choroidal plexus.

CASE 45 (Grandclement<sup>49</sup>) —Autopsy disclosed a cauliflower-like tumor, the size of a nut, in the left cerebellopontile angle. Microscopically the tumor was made up of delicate, sharply outlined growths of connective tissue containing blood vessels covered with epithelium in regular simple rows. "It resembles neoplasms of the choroid plexus."

#### SUMMARY

1. Two cases of papilloma of the choroid plexus are reported. In one the tumor was surgically removed from the left lateral ventricle with relief from symptoms. The second case represents the observation at

<sup>48</sup> Zalka, Edmund. *Histologische Veränderungen des Plexus chorioideus bei verschiedenen Krankheitsformen*. Virchows Arch f path Anat **267** 398 and 412, 1925.

<sup>49</sup> Grandclement A. *Tumeurs des plexus choroïdes du quatrième ventricule*, Lyon med **140** 136 1927.

necropsy of a huge papilloma of the choroid plexus with true "seeding" of the tumor via the cerebrospinal fluid

2 The reports of about forty-five cases have been collected from the literature which, so far as one can determine from the descriptions given, seem to have arisen from the choroid plexus. A few of these presented the phenomenon of "seeding"

3 The favorite site for these tumors is the fourth ventricle, 50 per cent were so situated, 34.7 per cent were in the lateral ventricles, and 17.3 per cent in the third ventricle. By some curious coincidence 93 per cent of tumors of the lateral ventricle have been on the left side

4 The age incidence was greatest in the first decade and gradually diminished up to the sixth decade

5 The surgical removal of this type of tumor is feasible, especially with the aid of electrosurgical devices. Preliminary roentgen treatment in my cases appeared to have reduced the vascularity greatly

6 A considerable part of the nonobstructive hydrocephalus found with tumors of the choroid plexus may well be associated with the increased epithelial surface



# SPONTANEOUS RUPTURE OF THE NORMAL SPLEEN <sup>1</sup>

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Spontaneous rupture of the normal spleen or of the apparently normal spleen is a rare condition. A search of the literature reveals only eight cases. Of these, six may be considered authoritative and two doubtful.

## CASES FROM THE LITERATURE

Shorsten <sup>1</sup> reported one case in 1919.

CASE 1—A man, aged 43, entered the hospital with the complaint of vomiting and severe abdominal pain about the umbilicus. The onset was sudden, six hours previously. A year and a half before this time, he had been buried in the trenches after which he had developed severe abdominal pain and had been sent to the hospital for three months. The pain had not returned after his discharge. Other than this his previous health had been good.

At the time of entrance, examination showed extreme abdominal pain and tenderness, no change in liver dulness, but signs of free fluid in the abdomen. At operation, fluid and clotted blood were found in the peritoneal cavity. The spleen was found nonadherent and bleeding from a rent in the capsule. The gallbladder contained many small stones but was left intact.

The spleen was dissected almost into two equal parts by the hemorrhage, the tear extending transversely from the convex surface to the hilum. There had been no stripping of the capsule. The absence of adhesions and scars, or stripping of the capsule, made it seem unlikely that the previous injury was responsible for the rupture.

The patient's recovery was uneventful.

One case was reported by Connors <sup>2</sup> in 1921.

CASE 2—A man, aged 38, an alcoholic, had bronchitis and was suspected of having pulmonary tuberculosis. For three months previous to his admission to the hospital he had nausea, constipation and pain in the right upper part of the abdomen. No injury had been sustained, and he had never had typhoid or malarial fever. At the time of entrance to the hospital, he complained of pain in the upper part of the left side of the abdomen.

Roentgen examination showed a stricture of the colon at the splenic flexure which was thought to be malignant. No stricture of the colon was found at operation. The spleen had a hematoma beneath the capsule and was removed. There was no active bleeding at the time of removal. Examination of the spleen showed the splenic tissue to be apparently normal. Except for the hematoma which practically bisected the spleen longitudinally, it was normal in size. No microscopic examination was made.

The patient recovered from the operation but three months later returned to the hospital with pain in the upper part of the abdomen, and examination disclosed

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<sup>1</sup> Submitted for publication, Sept. 3, 1929.

1 Shorsten W. W. Brit. M. J. **2** 844, 1919.

2 Connors. I. F. Ann. Surg. **74** 1, 1921.

a tumor mass in the upper part of the left side of the abdomen which proved to be a cyst, probably of the pancreas, resulting from the inclusion of a part of the tail in the ligature. Four years later, the patient died of pulmonary tuberculosis.

In 1922 Metcalfe and Fletcher<sup>3</sup> reported two cases.

CASE 3—A man, aged 21, developed a sudden severe pain in the left side of the abdomen, radiating to his left shoulder, he vomited and went into a state of shock. Several hours later, he developed paroxysmal pain in the left upper quadrant, accompanied by tenderness, but no rigidity or distention. He had a leukocyte count of 25 000. No history could be obtained of an injury, or of malarial or typhoid fever. He had had influenza and pneumonia a few years previously. He had had no gastric symptoms, and the Wassermann reaction was negative.

Splenectomy was performed, and the patient recovered. The spleen was apparently normal microscopically and macroscopically.

CASE 4—A man, aged 21, developed cramplike abdominal pain that radiated to the left shoulder, and dizziness. This pain came on following a large drink of cold water. On admission to the hospital, he said that he had had no previous serious injury or illness. The day after admission, he got out of bed but had a return of the abdominal pain and dizziness. He later developed more pain, shock and signs of internal hemorrhage. At this time, there was no rigidity or distention, but dulness was present in the flanks. The following day, he still had pain in the abdomen and shoulder and seemed in a little better condition. The dulness in the flanks had increased, however, and at operation blood was found in the peritoneal cavity. A clot was found about the spleen and splenectomy was performed.

The spleen was found to have ruptured on the convex surface, but microscopically and macroscopically it was otherwise normal. Recovery followed.

The fifth case was reported by Susman<sup>4</sup> in 1927.

CASE 5—A man, aged 53, seventeen hours before admission developed a sudden severe pain in the upper part of the abdomen as he bent down to lift a bucket of water, and became nauseated. He had previously been in good health until the last three months, during which he had flatulence and indigestion after meals. There was no history of typhoid, malaria or injury.

On examination, the patient appeared to be in a state of shock. The abdomen was boardlike, distended and very tender in the upper and left portions. The liver dulness was decreased and he had pain in the right shoulder as well as in the abdomen. A preoperative diagnosis of perforated peptic ulcer was made.

At operation the transverse colon was so greatly distended that puncture was necessary before exploration could be made. The pelvis contained blood that was seen to be coming from the spleen which was removed. About 10 or 12 ounces (295 or 355 cc.) was present in the peritoneal cavity but at the time of operation there was no active bleeding. The patient died three days after operation from paralytic ileus.

The spleen was normal in size, shape and consistency. There was a hematoma almost as big as the spleen itself beneath the capsule on the convex surface where there was a tear about 1½ inches long and ½ inch deep, transverse and midway between the upper and lower poles. The spleen was carefully dissected

<sup>3</sup> Metcalfe R. F. and Fletcher I. Z. *Ann Surg* 75: 180, 1922.

<sup>4</sup> Susman M. P. *Brit J Surg* 15: 47, 1927.

in a search for some abnormality but none was found" Examination of the other organs showed them to be normal

The sixth case was reported by Rhame<sup>5</sup> in 1928

CASE 6—A white man, aged 25, an electrician, was seized with a sudden sharp pain in the left upper part of the abdomen, just after finishing dinner. He vomited almost at once. Despite two purgatives, the bowels had not moved at 4 the next morning. He had had influenza seven years before but no other illness. No history of malaria, typhoid or injury was given.

At the time of entrance to the hospital, he showed mild shock, moderate distention of the abdomen, tenderness under the left costal margin and rigidity over the entire left side of the abdomen. Pressure over any part of the abdomen caused pain in the left upper quadrant. There was no pain in the shoulder. Analysis of the blood showed hemoglobin, 85 per cent, leukocytes, 13,040, and polymorphonuclear neutrophils, 85 per cent.

At operation about 750 cc of free blood was found in the abdomen, including clots. A rent was found in the outer surface of the spleen. Splenectomy was performed. The patient has remained well, with a practically normal blood picture.

Examination of the spleen showed it to be normal in size and appearance except for a tear in the capsule about the middle of the convex surface. The hemorrhage extended through the middle of the organ toward the root. Microscopically, the pulp was normal. The malpighian bodies were thickened. At one point the veins contained a beginning thrombus, but there was no reason to suppose that this thrombus antedated the hemorrhage.

The next two cases described may be regarded as doubtful. In 1874, Atkinson<sup>6</sup> described a case.

CASE 7—A woman, aged 35, had complained of epigastric pain and vomiting for five months. She developed severe pain in the left upper part of the abdomen, which radiated over the entire abdomen, and she frequently vomited. She died in a state of collapse twenty hours after the onset. At postmortem examination, a large clot and much fluid blood were found in the abdomen. The spleen was shrunken, pale and flabby, the lower pole being "muddy pulp." The other abdominal organs disclosed no abnormality.

In 1878, Skerritt<sup>7</sup> reported a case.

CASE 8—A man, aged 53, had complained of nausea, anorexia and pyrosis for two months. He had had an attack of severe nosebleed. He was admitted because of a second attack, showing signs of severe hemorrhage. No abnormality was found on abdominal examination. After being in bed for several hours, the patient became dyspneic and died within an hour.

At autopsy a large intraperitoneal hemorrhage was found, with a ruptured spleen, the tear being on the convex surface and 1 inch (2.5 cm) long. No microscopic examination was made. The spleen and clot weighed 26 ounces (737 Gm), but the weight of the spleen alone was not given. The substance was described as soft and pulpy, owing to postmortem changes.

5 Rhame, J. S. *Ann Surg* 88 212, 1928.

6 Atkinson. *Ann Surg* 2 403, 1874.

7 Skerritt. *Brit M J* 1 641, 1878.

## AUTHOR'S CASE

I have one case to add to those already cited

CASE 9—The patient was first seen on the operating table after the appendix had been removed, and free old blood had been found in the peritoneal cavity. A lower right rectus incision had been made. I continued this upward and



Fig 1—Longitudinal section of spleen, showing hematoma almost bisecting it



Fig 2—Convex surface showing elevation of capsule with hematoma beneath

explored the entire right side of the abdomen. The gallbladder was thick gray and adherent to the hepatic flexure. It was not disturbed. As no cause was found for the bleeding on the right side, I slipped my hand over to the left side and found the spleen to be boggy. The incision was closed and a high left rectus incision was made. The spleen was delivered found to be bleeding and excised. Blood was found throughout the entire abdomen.

The history obtained subsequent to the operation was as follows. On Jan 20, 1929, while sitting in a small chair, the patient developed a severe sticking pain in the left side below the costal margin. This gave him considerable difficulty in breathing. He thought that he was about to have a bowel movement and walked into the toilet. He had no movement, however, and about ten minutes after the onset of the pain he became faint and lay down. One-half hour later he got up and walked to his own home next door. The pain became less, although it was still present. It was more severe when the patient was lying down than when he was sitting up. From that time until January 25, when he was operated on, he still had pain, which was present at all times and increased when he breathed or moved about.

The past history was unimportant from an etiologic standpoint. He "had always been well," had had none of the ordinary diseases of childhood, and, except for an occasional attack of grip or cold lasting for a day or two, he could remember no time when he felt bad. He had not had malaria, typhoid, syphilis or any other chronic disease. He had had no gallbladder or other

*Blood Counts Subsequent to Operation*

Date	White Blood Cells	Red Blood Cells	Hemo- globin, per Cent	Color Index	Poly- morpho nuclears	Large Lym- pho- cytes	Small Lym- pho- cytes	Transi- tionals	Eosino- phils	Baso- phils
1/29/29	19,850	5,552,000	95	0.9	95	4	1			
1/30/29	19,200	5,821,000	95	0.8	89	10				1
1/31/29	26,100	5,776,000	95	0.9	87	13				
2/ 2/29	15,950	6,204,000	100	0.9	90	8	2			
2/ 4/29	23,225	5,600,000	95	0.8	91	5	1			
2/ 5/29	23,150	4,624,000	100	1.0	84	13			2	1
2/ 6/29	18,000	4,738,000	100	1.0	81	5	8		1	
2/ 7/29	21,950	4,992,000	95	0.9	82	12	2		1	2
2/ 8/29	22,350	5,672,000	95	0.8	81	5	8	3		1
2/ 9/29	20,150	5,150,000	100	1.0	82	11	5	1	1	
2/11/29	11,850	5,300,000	95	0.9	87	6	6	1		
2/12/29	16,680	5,160,000	95	0.9	87	8		2		
2/13/29	11,850	5,568,000	95	0.8	83	7	6	1	1	2
2/14/29	11,300	5,088,000	100	1.0	61	21	5	6	1	3
2/15/29	10,100	5,216,000	100	1.0	69	21	5	2		
2/16/29	11,100	5,218,000	100	1.0	65	22	8		1	1

abdominal symptoms. His mother died of carcinoma of the stomach, and one brother died of nephritis. He had stopped work four days previous to the onset of pain. He had had no accidents. He was a brickmaker.

On entrance to the hospital, examination disclosed moderate tenderness and rigidity over the entire abdomen, somewhat greater over the left upper quadrant, pain particularly about the umbilicus, a temperature of 100.4 F., and a leukocytosis of 18,200 with 80 per cent neutrophils. Examination of the blood made the day after operation showed a negative Wassermann reaction, Widal test and blood culture.

A report of the blood counts made for two weeks after operation are given in the accompanying table.

The spleen weighed 156 Gm. and measured 17 by 18 by 2 cm. Over the anterior upper third there was an elevated area 8 by 7 cm. in which the capsule was separated from the spleen and when opened exuded clotted blood. From this there was direct communication into the splenic tissue. A similar small area was noted on the opposite side. The remaining splenic tissue was of normal color and consistency. Section longitudinally showed a normal appearing spleen except for areas of hemorrhage.

Microscopic section showed an increase of the fibrous elements with marked thickening and hyalinization of some of the blood vessels.

The postoperative course was somewhat stormy. On the second day, he became distended and developed an acute dilatation of the stomach. About the tenth day, he had what seemed to be an attack of cholecystitis, and a week later while at home he had a second attack. From that time on he had been in good health.

## COMMENT

The symptoms, except for the history of trauma, were not unlike those of traumatic rupture, although on the whole they were less severe. Sudden severe pain in the upper part of the left side of the abdomen was the only symptom common to all cases. Vomiting was present in four cases, shock in four cases, dulness in the flanks in two cases, pain in the left shoulder in two cases and in the right shoulder in one, rigidity was present in three and tenderness in four cases. Distention was present in two cases. In none of the nine cases was the condition correctly diagnosed previous to operation.

Eight cases occurred in males and one in a female. The two patients with doubtful cases died without operation, and the ruptured spleen was found at autopsy. Six of the seven patients operated on recovered and one died. Death was due to paralytic ileus. One patient returned for operation three months later for a pancreatic cyst.

Spontaneous rupture of the pathologic spleen is not uncommon. Malaria<sup>8</sup> is the disease in which the spleen ruptures most frequently. Typhoid<sup>9</sup> is probably the next. Cases have been reported in hemophilia,<sup>10</sup> pregnancy,<sup>11</sup> tuberculosis,<sup>12</sup> acute infections<sup>13</sup> and a few other conditions.

Susman summed up the views on the causes of spontaneous rupture as follows:

## (1) Softening of all the structures of the spleen

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8 Rankin, W. *Brit M J* **2** 211, 1917. Ogilvie W. B. *Brit M J* **1** 200, 1916. Skevington, J. *Brit M J* **1** 571, 1920. Sheaf E. W. *Brit M J* **1** 767, 1920. Lutten, in Nothnagel. *Special Pathology and Therapy* p. 245. Turner G. G. *Lancet* **1** 799, 1917. Noland and Watson. *Ann Surg* **57** 72, 1913.

9 Connor and Downes. *Am J M Sc* **147** 332, 1914. Bryan. *Ann Surg* **1** 856, 1909.

10 Hammesfahr, C. *Zentralbl f Chir* **1** 1634, 1923. Friesleben M. *Deutsche Ztschr f Chir* **173** 45, 1922.

11 Stretton, J. L. *Brit M J* **50** 901, 1926. Simpson. *Edinburgh M J* **12** 268, 1866. Hubbard. *New York M J* **30** 75, 1879. Schwing. *Zentralbl f Gynäk* **4** 291, 1880.

12 Cannaday. *Tr South Surg & Gynec Assn* **27** 514, 1914.

13 Fieber, E. L. *Wien klin Wchnschr* **34** 581, 1921. Millar. *Brit M J* **2** 490, 1916. Diehl H. S. *Spontaneous Rupture of the Spleen Following a Carbuncle*. *J A M A* **82** 951 (March 22) 1924. Lampe. *Deutsche Ztschr f Chir* **44** 407, 1897.

(2) Congestion of the portal vein and its radicles and inability of the narrow splenic vein to accommodate itself

(3) Blood being thus forced between the spleen and the investing peritoneum which finally gives way and

(4) Perisplenic adhesions which by fixing the organ, predispose to rupture

That spontaneous rupture of the normal spleen ever occurs is denied,<sup>14</sup> but evidence from the eight ruptured cases and my own would seem to indicate that such a condition has occurred. Two theories may be entertained as causes of such rupture. The first is that the spleen is not normal in its entirety, but that the rupture occurs at a localized diseased area, and that this area is destroyed by the hemorrhage resulting from the rupture. The digestive juices of the stomach are decreased following removal of the spleen,<sup>15</sup> and probably the spleen supplies a substance the loss of which would cause the stomach to secrete less pepsin. From this Susman suggested that the disease of the spleen, as yet unrecognizable or localized, causes the disturbances of the digestive system. In support of this view, he wrote that of the seven cases reported up to the time of his article, "five patients had digestive symptoms, two had conditions in the other organs sufficient to account for these symptoms—namely, gall stones and tuberculosis respectively, in the remaining three no cause for the gastric symptoms was discovered." Of the two subsequent cases, that of Rhame disclosed no concurrence or previous disease, while mine showed evidence of a diseased gallbladder.

The second theory is that the rupture of the normal spleen is not spontaneous but traumatic. Lempriere<sup>16</sup> reported a case in which a small rupture of the spleen occurred, it stopped bleeding but eight days later during exercise rupture occurred for a second time.

Jackson<sup>17</sup> reported the case of a patient operated on twenty-eight days after injury to the left side caused by a desk at school. At the time of the injury, she felt only slightly unwell. Cases of traumatic rupture are reported in which the injury was not commensurate with the pathologic condition. The spleen may also be injured by indirect violence,<sup>18</sup> as that caused when a person twists to escape falling or when there is a sudden and violent contraction of the abdominal muscles.

The spleen is a contractile organ having systole and diastole. It also varies in size, increasing after eating. It has what may be considered a

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14 Ledderhose, in Billroth, and Luecke. *Deutsche Chirurgie*, Stuttgart, 1890, vol 45, p 147. Foucault. *Je de med de Bordeaux* **32** 1002, 1925.

15 Moynihan. Bradshaw Lecture, 1920.

16 Lempriere. *Brit M J* **1** 581, 1923.

17 Jackson, J. N. *Surg Gynec Obst* **41** 362, 1925.

18 Gordon-Watson. *Chouces System of Surg*, vol 2, p 3.

normal variation in size dependent on the load thrown on it by the necessity of eliminating blood cells and toxic products

Six of the nine patients gave a possible history of indirect violence. Of these, two had nausea and vomiting, one nausea and retching and one experienced strain from reaching down to lift a bucket of water. The other two had bronchitis. It is not stated that the rupture occurred during coughing or retching, but it is possible that as these complaints had been present for a long time and were of frequent occurrence they were not associated by the patients with the onset of the pain. In the other three cases, there is no history of any form of trauma.

In my case, the spleen ruptured while the patient was sitting quietly in a chair. Two patients had definite disease of the gallbladder without symptoms. One had eaten a heavy meal just before the rupture and another had had a large drink of cold water. Two had had gastric symptoms without demonstrable pathologic change; in one the history was altogether negative, and in one a beginning thrombus was present.

A diseased spot in the spleen may have caused some of these ruptures, recent trauma, others and remote injury still others, but on the basis of the evidence presented I do not feel that spontaneous rupture of the normal spleen may be considered nonexistent.



# MULTIPLE MALIGNANT ADENOMAS OF THE KIDNEY \*

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AND

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Large adenomas of the kidney are rarely reported in the literature, but small tumors of this type varying in size from 2 mm to 2 cm are often found at necropsy. Kretschmer<sup>1</sup> recently reviewed seventeen cases of the former type in the literature and added a case of his own. We are reporting another case, the third in which operation was performed and the third reported from the Mayo Clinic.

## REPORT OF A CASE

A man, aged 46, came to the Mayo Clinic complaining of stomach trouble, weakness, constipation and a palpable tumor in the left hypochondrium. His father had died of carcinoma of the rectum at the age of 60. The patient had malaria in 1894, and in 1909 he had a "nervous breakdown" and a hemorrhoidectomy was performed. He stated that since he was 20 years of age he had had severe indigestion, characterized by gaseous distention, nausea and epigastric heaviness. Because of constipation he had required cathartics daily for years. During the last six months, the weakness had become progressively worse. Two weeks prior to examination, he consulted his family physician because of the dyspepsia. At that time, a tumor was found in the left side of the abdomen, and a roentgenogram was advised.

The patient appeared to be nervous and frail. His height was 5 feet 5 inches (165 cm), and his weight, 120 pounds (54 Kg), he claimed this was his usual weight. The pulse rate was 90, the temperature was 97.8 F. The systolic blood pressure was 118 and the diastolic 78, measured in millimeters of mercury. There was a brown patchy discoloration of the skin in the regions of the axilla, groin and buttocks. Anteriorly, a mass extended from the left costal arch almost to the iliac crest. This extended posteriorly into the costovertebral angle, and moved with respiration. It was firm and painless and irregular in outline. The region of the right kidney was normal on palpation, but had a large varicocele on the left side. The specific gravity of the urine was 1.016, the reaction was acid, and the albumin was graded 1. There was an occasional pus cell in each low-power microscopic field. The blood urea was 22 mg in 100 cc. The hemoglobin was 81 per cent, the erythrocytes numbered 5,070,000, and the leukocytes numbered 7,100. The Wassermann reaction of the blood was negative. A test meal showed

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\* Submitted for publication, Aug. 3, 1929.

1 Kretschmer, H. L., and Doehring, C. Adenoma of the Kidney, *Surg. Gynec. Obst.* **48**: 629, 1929.

2 Foulds, G. S., Scholl, A. J., and Brusch, W. F. A Study of Histology and Mortality in Renal Tumors, *S. Clin. N. Amer.* **4**: 407, 1924. Judd, E. S., and Simon, H. I. Benign Adenoma of the Kidney, *Surg. Gynec. Obst.* **44**: 169, 1927.

the total gastric acidity to be 40 and free hydrochloric acid 16 in a total quantity of 80 cc. Roentgenograms of the chest and stomach were normal. A roentgenogram of the kidneys, ureter and bladder disclosed a large shadow in the region of the left kidney, and a spina bifida of the fifth lumbar vertebra. Examinations showed that the eyes, ears, nose and throat were normal. Three teeth showed evidence of periapical infection.

Cystoscopy revealed a normal bladder and normal ureteral meatuses. Clear spurts of urine appeared from each ureter. Catheters passed to each kidney without difficulty. Specimens of urine, collected from the kidneys through catheters in the ureters, did not contain pus. A few blood cells were present but were

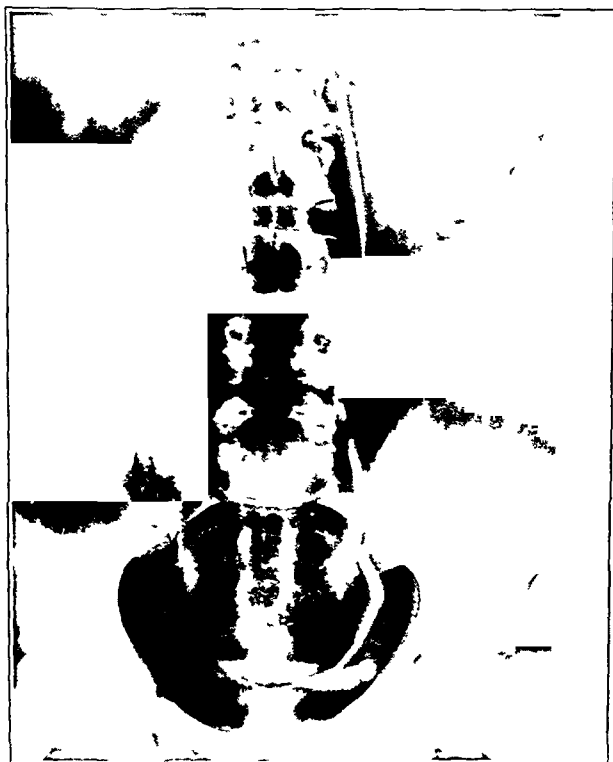


Fig 1—The left pvelogram shows the outline of a large pelvis with the superior and inferior calices unusually broad and somewhat elongated. The middle calix is abbreviated. The outline of the lower calix is irregular in density, suggesting cortical pressure. The kidney is large.

assumed to be traumatic in origin as a second specimen from the left kidney did not contain blood. Indigocarmine injected intravenously appeared in four minutes from each ureter with concentration graded 4. A pvelogram was made on the left side (fig 1) and showed the outline of a large renal pelvis with the superior and inferior calices unusually broad and somewhat elongated. The middle calix was apparently abbreviated. The lower calix was irregular in density suggesting cortical pressure. The diagnosis was indeterminate but a polycystic kidney or a single cyst of the lower pole was considered. A pvelogram was then made on the opposite side which was negative thus excluding polycystic disease. A differential intravenous phenol-sulphonphthalein test showed a normal return from each



Fig 2—The posterior surface of the left kidney shows normal substance in the center with the largest tumor attached to the lower pole. The capsule has been removed from the tumors and the kidney.



Fig 3—A cross-section of the kidney shows multiple adenomas, the largest is 12 cm in diameter. Normal renal tissue seen on the left is being compressed by multiple adenomas. A small adenoma may be seen in the cortex of renal tissue.

kidney. A urologic diagnosis was made of the tumor of the left kidney, evidently a solitary cyst of the lower pole, with unimpaired renal function. Exploration of the left kidney was advised.

The gastro-intestinal symptoms were explained by the constipation, with possibly a secondary relationship to the renal lesion. Pigmentation of the skin suggested hyposuprarenalemia associated with the renal condition, but because the blood pressure was not low, this was considered unlikely.

At operation a left oblique lumbar incision was made. The kidney was about five times the normal size, nodular in shape, and moderately adherent to the surrounding tissues. At the lower pole was a large rounded tumor, and multiple

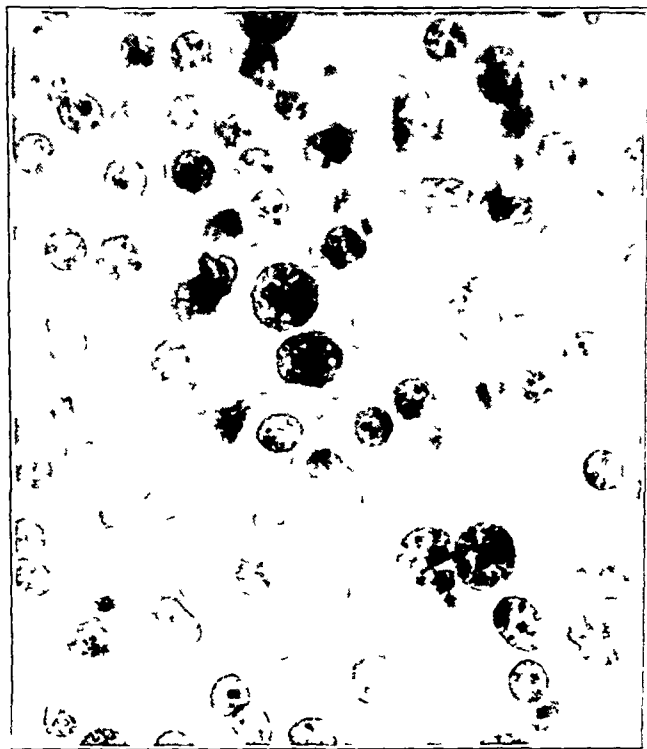


Fig. 4—In the center and right lower quadrant are definitely malignant cells with large nuclei and multiple large nucleoli,  $\times 250$

firm, smaller nodules surrounded the kidney. As the mass was retracted forward and upward, there appeared to be a small amount of renal tissue remaining on the posterior aspect. The pelvis, ureter and vascular pedicle were in practically their normal positions. The ureter was cut at about 5 cm. distal to the pelvis, ligated and dropped back. The vascular pedicle was cut and doubly ligated.

#### PATHOLOGIC DATA

The kidney was about five times the normal size (fig. 2). When sectioned through the long axis (fig. 3) the capsule stripped with difficulty. On the cut surface there were five distinct grayish red tumors, the largest 12 cm. in diameter, all surrounding a small amount of normal appearing renal tissue. In the cortex

of the kidney just beneath the capsule were two small tumors, 3 and 5 mm in diameter. There were several trabeculated areas of white shiny material resembling connective tissue which radiated from near the center of two of the tumors. One tumor also had a dark area that appeared to be the result of hemorrhage.

When the capsule was stripped from the mass, the renal substance radiated over the surface of the tumor until it became so thin that it appeared to act as the capsule of the tumor. Each tumor appeared to be encapsulated and definitely benign, but on microscopic examination this was shown not to be the case.

Microscopically, tumorous tissue was seen in juxtaposition to renal tubules and glomeruli (fig 4). The tumor, however, did not have a capsule, tumorous



Fig 5—Normal renal tissue may be seen in the upper left corner of the section. The tumor is in the lower right part of the field with no intervening capsule. Renal tubules have been compressed in the area between the tumor and the kidney,  $\times 150$ .

cells adjoined normal renal cells. There was evidence of cortical pressure as the blood vessels and tubules, and the glomeruli were flattened near the tumor. The arrangement of tumorous cells was roughly adenomatous. The cells were polygonal and resembled columnar epithelial cells, they were slightly irregular in shape. A moderate degree of differentiation was present. The cells and their nuclei were larger than normal renal cells. Large nucleoli and deeply staining granules were present, appearing to be definitely malignant cells (fig 5).

# CASE REPORT

The patient had practically no symptoms referable to the large renal adenoma. He had also several multiple cysts, seven 0.5 to 1.2 cm. in diameter. The kidney was markedly compressed, but the renal function remained normal.

The category of neoplasia of the kidney is not known. Whether they are malignant or are capable of undergoing malignant degeneration is important. It was formerly believed that the tumors were all benign. At present, however, certain pathologists believe they are malignant. The degree of malignancy varies, but usually it is relatively low. In the small adenomas found at necropsy, the degree of malignancy is low, but if the patient were to live long enough a large tumor would probably develop. The large tumors usually found in younger persons are more malignant, and closely resemble adenocarcinoma or hypernephroma. In other words, all adenomas of the kidney belong to the so-called hypernephroma type which is important to the surgeon from a therapeutic standpoint. As illustrated in the case presented, small tumors may be present in the renal cortex with large tumors. Should the tumor be resectable in a manner that would leave a functioning kidney, this would seem to be the procedure to carry out. If one keeps in mind the possibility of multiple tumors and of malignancy, nephrectomy would seem to be the best plan if the opposite kidney is normal. It is not possible to determine how long tumors of this type have been present in a given kidney. Growth must be very slow in most cases. Following resection of one pole of a kidney for adenomas, one patient was known to be alive and well eight years later.<sup>1</sup> In another case, two years following nephrectomy for a similar type of neoplasm, the patient is known to be alive and well.<sup>2</sup> There is no evidence in the literature that the tumors metastasize, but the microscopic appearance leads one to believe that they would if the tumor was allowed to grow for a sufficiently long time.

# EWING'S SARCOMA

SMALL ROUND CELL SARCOMA OF BONE<sup>†</sup>

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AND

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BALTIMORE

WITH FOREWORD BY

JOSEPH COLT BLOODGOOD, M D

BALTIMORE

## FOREWORD

It is important to record here again that Dr Copeland and Dr Geschickter were research fellows in the Surgical Pathological Laboratory of the Johns Hopkins University and Hospital for six months only, ending Jan 1, 1929. Previous to entering on this investigation on tumors of the bone, they had studied the bone material and published in the ARCHIVES OF SURGERY a comprehensive investigation of multiple myeloma. This work was performed while they were medical residents at the Baltimore City Hospital under the supervision of my colleague, Dr Boggs, and I should like to record here my appreciation of the aid and opportunities that he gave these two young medical graduates. During these six months every tumor of the bone, benign and malignant, and every example of disease of the bone, were studied comparatively, first microscopically and then in the gross and by roentgen and clinical pictures. To make this investigation even more comprehensive, all the benign and malignant connective tissue tumors of soft parts, tendon sheaths, bursae and joints were gone over in the same critical way.

On January 10, two papers by Drs Geschickter and Copeland were presented before the Johns Hopkins Medical Society and discussed by Dr James Ewing of New York. The first paper was on "Osteitis Fibrosa and Giant Cell Tumor" and was published in the ARCHIVES OF SURGERY, the second was the present paper on the nature of Ewing's tumor. I have before me a third paper giving the results of their study of the metastasizing and recurrent giant cell tumor. A fourth paper, on osteogenic sarcoma, is almost ready for publication.

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\* Submitted for publication, Dec 27, 1928

\* From the Department of Surgery and the Surgical Pathological Laboratory of the Johns Hopkins Hospital and University

\* Aided by a grant of the Hartley Corporation

In discussing the two papers before the Johns Hopkins Medical Society I was asked by one of my colleagues whether I had told the authors all the new things they brought out in their papers. My answer should be published here—No. Dr. Geschickter and Dr. Copeland may be given credit for everything that deserves credit in this series of articles on lesions of the bone and it is my opinion that they have made valuable and helpful contributions.

The medical profession of this country is listening in for any correct information which will help them to interpret properly and treat intelligently lesions of the bone. As the experience of those who see the largest number of patients annually grows the difficulties of diagnosis increase. This is directly due to the fact that the people are so universally and so well informed that they seek a roentgen study the moment they are aware of any symptom referred to a bone or joint. The clinical picture that was helpful in the past is rarely alone helpful today. The roentgenogram in the early stage of the disease in many instances reveals a new picture. In addition when biopsy is necessary even trained pathologists are sometimes unable to differentiate between benign and malignant lesions. Roentgenograms are being taken for apparently trivial conditions and after all slight contusions of the bone or sprains of joints so that healed or latent diseases of the bone are being brought into view with which as yet surgeons have little familiarity.

Let me give a few examples from the past year. A postgraduate student was in the roentgen department when a new Coolidge tube was being tested and offered her leg for a roentgen examination. There had been no symptoms on the part of the fibula. The developed plate showed what was interpreted as a partially healed cyst of the bone in the shaft of the fibula. Up to the present time I have no record of a primary or metastatic malignant tumor being so revealed by purest accident but about seven years ago, in a roentgenogram of a knee-joint made because of symptoms suggesting tuberculous arthritis, a calcified area was found in the outer condyle of the femur, it was interpreted as healed tuberculosis or ossified bone cyst and for this reason was not explored. Three years later, I was compelled to amputate this leg for a myxosarcoma, and the patient is now dying of metastasis. It is fair to conclude that if the area had been explored and radically removed, the patient would probably be cured, perhaps without the loss of the limb. On a few occasions, I am inclined to the view that the apparent cure of a lesion of the vertebra diagnosed as a metastasis from cancer of the breast is due to the fact that the disease of the vertebra is caused by tuberculosis or an old fracture. In a patient with Paget's disease of the skeleton and a history of the removal of both breasts for cancer fifteen years previously, there was nothing in the roentgenogram of the skull to suggest the metastasis later found at biopsy.



A recent roentgenogram of the shaft of the tibia in a child, taken because of a lesion that suggested a cyst of the bone, disclosed a malignant aneurysm of the bone lined by osteogenic sarcoma tissue, while another suggesting a malignant tumor proved to be a benign cyst of the bone. A destructive lesion in the ilium diagnosed as primary or metastatic malignant disease proved at biopsy to be granulation tissue. Three months ago, one of my colleagues who is experienced in roentgen diagnosis referred to me a patient with a lesion of the upper shaft of the femur, a positive diagnosis of osteogenic sarcoma had been made, and the patient requested advice as to irradiation or amputation. Subsequent events proved the condition to be osteomyelitis, and the patient was relieved without irradiation or amputation.

Studies of the type of those of Drs. Geschickter and Copeland, based on large series of cases, are therefore welcome. But it must be remembered that the clinical, roentgen and gross pictures are of types of sarcoma of bone observed during the past thirty-nine years. The only uniform observation is a histologic one. Yet, when one compares the sections in these sixty cases of round cell sarcoma arising in the shaft of bones of patients from 4 to 44 years of age with round cell sarcoma of the soft parts, it requires considerable experience to differentiate them. Nor is it always easy, with the microscope only, to pick out with certainty Ewing's sarcoma from multiple myeloma, from some of the cases of chondrosarcoma, from endothelial angiosarcoma and from the granulation tissue of periostitis or osteomyelitis. It is therefore important for pathologists to familiarize themselves with this histologic picture, because as lesions of bone come under observation, it becomes more and more difficult to recognize the nature of the disease from the roentgenogram, with the help of the clinical picture and all other laboratory investigations. Biopsy at the exploratory incision will have to be employed more and more often, until studies of this character in a larger number of more recent cases make it possible to obtain some clue to a more correct diagnosis from the roentgen examination.

In conclusion, it is important to record here again, as I have frequently done before, the safer working rules for the diagnosis of and the treatment for lesions of the bone.

- 1 If the roentgen and the clinical pictures are obscure and help is wanted in interpretation, do not perform biopsy and send the sections to other departments for examination, but refer the roentgenogram and a report of the clinical picture.

- 2 While waiting for the diagnosis, keep the part at rest in bed in crutches or a sling, and give the patient roentgen irradiation. The best results are being obtained with daily treatments for twelve days. Such treatment never does harm. It makes it possible for one to tell whether the lesion is radiosensitive—a valuable point often emphasized by Dr. James Ewing of New York.

The patient had been treated with antibiotics for several months before the diagnosis was made. The patient was in good health and had no other symptoms. The patient was treated with antibiotics for several months before the diagnosis was made. The patient was in good health and had no other symptoms. The patient was treated with antibiotics for several months before the diagnosis was made. The patient was in good health and had no other symptoms.

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Do not neglect the clinical history. It is quite possible that as the number of carefully recorded clinical histories of the earliest stages of all types of lesions of bone are increased, valuable differentiating data may again be brought to life.

Do not neglect palpation. Repeat it. It is quite true that the older descriptions of the palpation of benign and malignant lesions of bone no longer hold good, but I am finding new data when palpation is repeated. For example, when palpation was performed on the patient already referred to who had a lesion of the upper third of the shaft of the femur diagnosed roentgenographically as sarcoma, a spindle swelling was found surrounding the femur below the lesser trochanter for a distance of 6 cm. This is the usual manifestation in periosteal sarcoma. There was certain evidence in the roentgenogram that suggested

osteomyelitis. Abscesses at the roots of teeth and infected sinuses were found. After these foci of infection were treated, the encircling spindle-shaped periosteal mass quickly subsided, leaving only on the outer side in the fascia lata a small doughy mass the size of a dollar, as this quickly became detached from the femoral bone, my associates and I were confident from palpation alone that this could not happen in sarcoma. A few days later, this area was explored and a tiny sequestrum was found in a cavity lined by granulation tissue and without pus. Again, the frozen sections of this granulation tissue suggested sarcoma, but organisms in the smears and later cultures practically excluded sarcoma. This sequestrum showed in the roentgenogram. It was not larger than 2 by 3 mm. The finding of this in the first roentgenogram was looked on as evidence against sarcoma.

5 In these cases of sarcoma of the bone in its early stages, there is now evidence of positive cures being effected by resection instead of by amputation, a few by curetting and irradiation and a few by irradiation alone.

In preparation for a demonstration before the Chicago Roentgenological Society, I recently reviewed with a group of special students all our lantern slides on lesions of the bone, and I found that Copeland and Geschickter recorded eight five-year cures in Ewing's tumor, a percentage of almost 13. In 1921, I could record only two five-year cures among fifty-two cases of sarcoma of all types—less than 4 per cent of the total. This great increase of permanent cures is dependent largely on earlier intervention. Every patient cured by irradiation alone, of course, could have been cured by resection or amputation. There is no evidence as yet that irradiation has cured any patient with sarcoma of the bone with metastasis to the lungs.

It is my observation that Ewing's sarcoma of the bone is more radiosensitive than any other type of sarcoma of the bone, and this is why irradiation should be tried first in all doubtful cases.

I can add the following cases to those already recorded by Copeland and Geschickter. First, there is a patient now well seven years after treatment with irradiation alone. The tumor occupied the upper half of the shaft of the humerus. To have removed it would have required a shoulder-girdle amputation. There is no proof, except the suggestive x-ray picture, that it was a Ewing tumor.

Almost three years ago, Dr. Campbell of Memphis explored a lesion of the lower third of the fibula. Roentgenographically, the lesion was typical of periosteal sarcoma with involvement of the shaft, with both formation and destruction of bone. The section obtained at biopsy showed a Ewing round cell sarcoma. This patient is clinically well. The roentgenograms now show a healed lesion.

More than four years ago Dr Watkins of Birmingham referred to me the roentgenograms and tissues of a sarcoma of the shaft of the tibia, microscopically, it was a Ewing sarcoma. Nothing was done beyond curetting and irradiation. The clinical and roentgen pictures now record a healed lesion.

When I go over the records of all sarcomas of the bone there is no doubt that more patients in the group with Ewing's sarcoma were radiosensitive and that in a few the condition was temporarily checked by this treatment.

It is interesting to record again that in the cases in the records there is not an example of a five-year cure after amputation for a lesion of the upper extremity or above the middle third of the femur but there are now five examples of patients with different types of sarcomas of the bone situated in the upper extremities who have remained well after resection. At the present time I myself would prefer resection to irradiation alone, but if the tumor is situated in the upper extremity or above the middle third of the femur and its local growth prohibits resection, irradiation should be the treatment of choice.

The actual results of conservative treatment for sarcoma of the bone cannot be written today. In a few years sufficient material will have been amassed so that one can decide between amputation, resection curetting, with and without irradiation and irradiation alone. There is little evidence that any treatment will affect or cure metastasis to the lung.

*Ewing's Sarcoma*—Before the publication of the article by my colleague Dr Ewing these sarcomas of bone were differentiated from the osteogenic and other types of sarcoma as periosteal round cell sarcoma or alveolar sarcoma. I agree with Dr Copeland and Dr Geschickter that they are justified in picking out these 60 cases to be classed as Ewing's tumors from among the 400 examples of sarcoma of bone. I am inclined to feel that future studies will demonstrate that in the earliest stages this tumor cannot always be segregated by the clinical or roentgen picture but the demonstration of radiosensitivity will be suggestive of this peculiar round cell sarcoma and biopsy will also reveal a typical histologic picture. Let me again repeat a warning. The granulation tissue periosteal or endosteal in osteomyelitis whether syphilitic pyogenic or traumatic, will closely resemble Ewing's sarcoma.

## EWING'S SARCOMA

By Drs COPELAND AND GESCHICKTER

Since the introduction of the term endothelioma by Golgi<sup>1</sup> in 1869 various authors have valued this term as a pigeon-hole for many odd

<sup>1</sup> Golgi C cited by Simon W V. Die Knochen-sarcom. Ergebn d Chir u Orthop. 16:341. 1923

and unusual tumors the origin and histologic relations of which are still but on the horizon of biologic investigation

From time to time various tumors have been described as endothelial in origin Billroth<sup>2</sup> in 1856 described a tumor in this category which he called cylindroma, and Waldeyer<sup>3</sup> later linked the term angiosarcoma with tumors classed as endothelial Kolazcek<sup>4</sup> in 1878, and again in 1880, in an extensive study, drew a comprehensive picture of such tumors under the term angiosarcoma The present tendency, however, is to limit the term angiosarcoma to angiomatous tumors in which the unit is the blood vessel and not the endothelial cell The term perithelioma has also been used to designate the origin of many malignant tumors, as certain types of angiosarcoma, the term being given special prominence by Hildebrand<sup>5</sup> in regard to certain tumors of bone

Against such classifications in which comparatively few recognized groups are supported by satisfactory data, among the older authors Ribbert<sup>6</sup> may be considered outstanding He expressed the view<sup>7</sup> that the endothelial origin of certain tumors of the bone has yet to be proved, and, further, that the mere continuity of the tumor cells with endothelial structures at the margin of the tumor is no proof of their identity The proof of such an identity rests on the study of the tumor at its inception or at its original formative site In recent years, Ewing<sup>8</sup> adopted the conception of Boist that the scope of endothelioma is probably wide, allowing him to give full expression to the views of many who favor the endothelial origin of a wide variety of tumors the exact nature of which has not been determined With this idea in mind, Ewing selected from among the malignant tumors of the bone a nonosteogenic tumor with many clearcut clinical features, placing it within the realm of endothelial tumors, known as endothelial myeloma<sup>9</sup> or diffuse endothelioma<sup>10</sup>

2 Billroth Untersuchungen über die Entwicklung der Blutgefäße, Berlin, 1856

3 Waldeyer Die Entwicklung der Carcinome, Virchows Arch f path Anat 55 67, 1872

4 Kolazcek, J Ueber das Angiosarkom, Deutsche Ztschr f Chir 9 165, 1878

5 Hildebrand Ueber das tubulare Angiosarkom oder Endotheliom des Knochens, Deutsche Ztschr f Chir 31 263, 1891

6 Ribbert, H, cited by Ewing, J Neoplastic Diseases, ed 3, Philadelphia, W B Saunders Company, 1928, p 333

7 Ribbert H, cited by MacCallum, W G A Textbook of Pathology Philadelphia, W B Saunders Company, 1928, p 930

8 Ewing, J Endothelial Myeloma of Bone, Proc New York Path Soc 24 93, 1924

9 Ewing J A Review and Classification of Bone Sarcoma, Arch Surg 4 485 (May) 1922

10 Ewing J Neoplastic Diseases, ed 3, Philadelphia, W B Saunders Company 1928, p 351

of the bone Connor,<sup>11</sup> in a recent study of the bone material with the Codman Registry, supported Ewing in this view, and Kolodny,<sup>12</sup> in a similar treatise, agreed with Ewing that the tumor presents a clearcut entity, but he did not feel that the contention that it arises from perivascular endothelium was well grounded. McCallum,<sup>13</sup> in a more emphatic way, placed the burden of proof on the investigator who designates any tumor as endothelial in origin, yet felt that in certain instances descriptions of true endotheliomas had been recorded, and he cited such instances in his textbook of pathology.

At the suggestion of Dr J. C. Bloodgood, the entire collection of tumors of the bone, both benign and malignant, in the Surgical Pathological Laboratory of the Johns Hopkins Hospital (representing, in all, a total of over 1,500 cases together with 1,000 cases of diseases of bone), was made the subject of a comparative histologic study. Later the observations thus obtained were correlated with the clinical data, the gross material and the x-ray pictures. For purposes of microscopic analysis, the tumors were studied and classified according to their cellular elements, stroma and special areas, the special areas connoting old bone, healing bone, hemorrhage, pigment, necrosis, etc. Symbols were given these different elements for the sake of brevity and from the standpoint of standardization in classifying tumors. From among the cases of malignant tumors of the bone, a series of sixty, which were grouped under the name of periosteal round cell sarcoma or Ewing's endothelial myeloma, were selected for the present analysis. The study includes thirteen full case reports on patients admitted to the surgical service of the Johns Hopkins Hospital.

#### ETIOLOGIC FACTORS

Ewing's sarcoma<sup>14</sup> is essentially a disease of early life, 95 per cent of the cases in this series occurred in persons between the ages of 4½ and 25. In this respect, it does not differ from other sarcomas of bone, the majority of the cases of which occur in the first two decades of life. The youngest person whose case was reported in our series was a child aged 4½, while the oldest was a white woman aged 44, although Connor reported a case in a patient aged 60 (fig. 1).

Among the 400 sarcomas of the bone in the Surgical Pathological Laboratory of the Johns Hopkins Hospital 15 per cent were found

11 Connor, C. L. Endothelial Myeloma. *Ewing Arch Surg* **12** 789 (April) 1926.

12 Kolodny, A. Bone Sarcoma. *Surg Gynec Obst* **44** 126 1927.

13 McCallum, W. G. A Textbook of Pathology. Philadelphia: W. B. Saunders Company, 1916, p. 928.

14 Codman, E. A. The Nomenclature Used by the Registry of Bone Sarcoma. *Am J Roentgenol* **13** 105 1925.

to be Ewing's sarcoma. Males affected predominated over females in an approximate ratio of two to one (thirty-nine males and twenty-one females). With relation to color, the tumor was apparently rare in all races save the Caucasian, only one case in the series occurred in a negro.

Trauma was recorded in twenty-two cases, although the actual number in which it occurred was probably greater, since in many instances trauma was not sought for or was not recorded. In every case in which trauma was recorded, the trauma was definitely related to the subsequent onset of the clinical symptoms. The average lapse of time between the trauma and the onset of clinical symptoms was approxi-

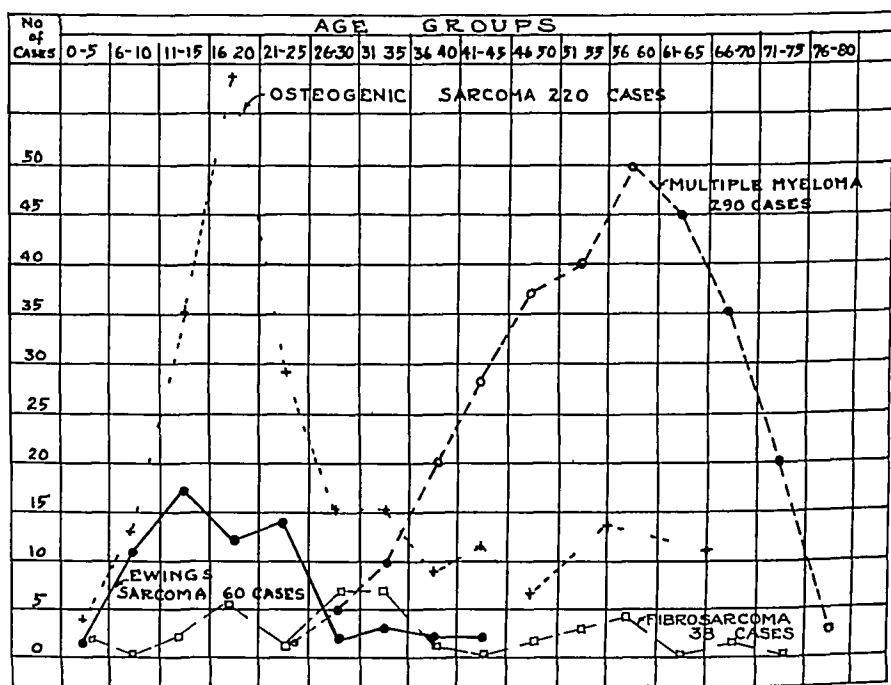


Fig 1—Age incidence of Ewing's sarcoma, compared with age incidence of other malignant lesions of bone

mately five and one half months, the extremes being a few days and a year or more.

In considering trauma as an etiologic factor, the question always arises whether the injury was superimposed on an already existent tumor or whether it actually was the stimulus to production of the malignant growth. There are some grounds for assuming either conclusion, but in our series the majority of such injuries reported undoubtedly preceded the disease.

#### CLINICAL CHARACTERISTICS

*Pain*—Pain was an outstanding symptom in fifty cases (83 per cent) and was noted as the first symptom in twenty-one cases (35 per

cent) In most cases, pain began spontaneously, it followed trauma at times by a more or less short period, often appearing simultaneously with the formation of the tumor

In twenty cases, pain had been present for from five weeks to seven months before the patient came under observation and in nine cases it had been present for from one to two and one half years prior to clinical observation

A wide variation in the severity of the initial pain was apparent in some cases it was cramplike while in others it was either a sharp shooting pain or an aching only on motion Most frequently the pain was intermittent, lasting for from a few hours to several days, subsiding at intervals, only to recur with increasing severity The intervals between the attacks of pain became shorter in duration until a constancy of discomfort was noted by the patient, the pain at certain times being accentuated Nocturnal pain was the most severe, in many cases A pain concomitant with the appearance of tumor was not an unusual observation, remaining constant until spontaneous regression of the tumor occurred or until some operative intervention was resorted to

The characteristic course of the pain may be summed up as follows

Stage 1 Tenderness or soreness following trauma or arising spontaneously on motion

Stage 2 Intermittent pain of a dull, aching or sharp shooting character, lasting from a few hours to several days

Stage 3 Periods of freedom from pain

Stage 4 Continuous pain either of a dull aching or sharp shooting nature appearing with progression in the size of the tumor or spontaneously and subsiding after regression in the size of the tumor or after operative or x-ray treatment

In almost every case in which sufficient data were available two or more of these stages were noted

*Tumor*—In 56 cases (90 per cent) a mass could be palpated and in 19 per cent of the cases a swelling was complained of as the initial symptom The average duration of the formation of the tumor, as observed clinically or by the patient himself was thirteen and one-half months the periods ranging from three months to two years One exception to the period of tumor formation mentioned is of interest namely a case under observation in which there was a history of tumor extending over a period of seven years the tumor showing many regressions and recurrences prior to the patient's admission to the hospital

In only two cases was tumor the only manifestation of the disease In the majority of the cases trauma pain and tumor or pain and tumor were the syndrome In many cases the tumor was preceded by pain or trauma for a period ranging from two months to one year



The tumor masses varied from small localized swellings to large fusiform masses extending along almost the entire length of the affected bone. There were vasomotor changes about the growth, in many cases. The soft parts about the tumor in most cases were freely movable, but often were edematous, while in other cases there was only dilatation of the peripheral veins over the tumor without any disturbance of the fluid exchange in the tissues. In many instances there was a local elevation of the temperature over the tumor mass.

On palpation, the majority of the tumors presented an indurated swelling with a surface ranging from rough and irregular to smooth, and totally immobile, apparently continuous with the bone. Fluctuation of the tumors was not noted, though there were varying degrees of resilience all being less hard than bone. Many of the tumors were tender on palpation.

TABLE 1—*Bone Involvement*

Bone Involved	Total Number of Cases	Cases in Upper Shaft	Cases in Lower Shaft	Cases in Mid Shaft
Tibia	15	6	3	6
Femur	13	5	7	1
Humerus	7	4	1	2
Fibula	8	3	2	3
Radius	1		1	
Ribs	1			1
Pelvis *	5			
Scapula	4			
Clavicle	2			
Metatarsal	2			
Tarsal	1			
Skull	1			

\* Ilium four cases and one case undetermined

A peculiar feature in some of the tumors was their tendency to spontaneously decrease in size, with a sudden cessation of pain, and thus to disappear and reappear until some remedial treatment was instituted. Perhaps the variability in the size of the tumor at various times had to do with hemorrhage and the absorption of hemorrhage.

The bones most frequently involved were those of the long pipe bone class (table 1), although in a few instances the ilium, scapula, clavicle, skull and bones of the feet were affected (fig 2). In no case was the primary location of the tumor on other than the shaft side of the bone, where the long bones were involved. No predilection of the tumor for the right side or the left side of the body was noted, twenty-two cases occurred on the left side and twenty-three on the right side of the body. Those bones that are most readily subjected to trauma were the ones most frequently affected, i.e., the femur, tibia, humerus, fibula and pelvis, the tibia leading the list with an involvement in fifteen cases of this series.

*Fracture*—Pathologic fracture is of relatively rare occurrence in Ewing's sarcoma. It was noted in only three cases of this series, or 5 per cent. These fractures were of the femur, two occurring in the upper shaft and one in the lower shaft. Of all the malignant tumors of the bone, Ewing's sarcoma presents the minimal number of cases complicated by pathologic fracture. As was pointed out by the authors<sup>15</sup> recently, multiple myeloma heads the list of malignant tumors of bone in this respect with pathologic fractures in 62 per cent. Other

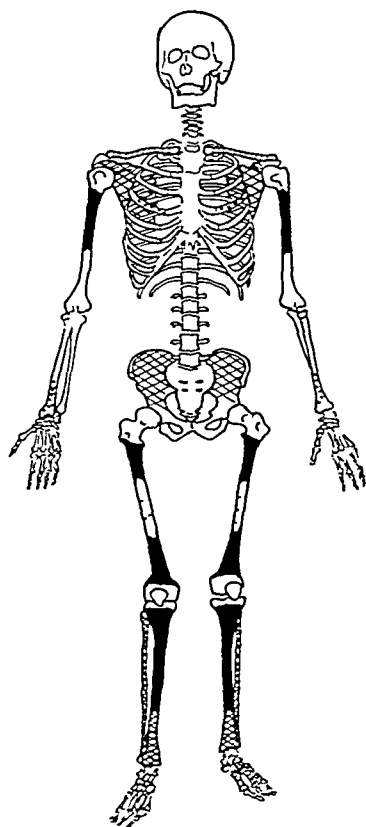


Fig. 2—Incidence of Ewing's sarcoma according to skeletal location. The solid black areas indicate the most frequent sites, the checked areas, the common sites, the diagonal lines, the occasional sites and the dotted areas, rare sites. The areas in white were not involved by tumor in this series.

bone tumors similarly affected by fracture are in the order of frequency, bone cysts 45 per cent, giant cell tumor 14 per cent and general sarcoma of bone 8 per cent. The low frequency of

15. Geschickter, C. F. and Copeland, M. M. Multiple Myeloma. Arch. Surg. **16**: 807 (April) 1928. Osteitis Fibrosa and Giant Cell Tumor. Ibid. **19**: 181 and 201 (Aug.) 1929.

pathologic fracture in round cell sarcoma is against the current opinion that this tumor is a primarily bone-destructive neoplasm, although pain of the affected part (due to weight bearing) may, in some instances, have saved the limb from this complication

*Constitutional Reaction*—The consideration of fever was handicapped by the sparsity of information in many of the case histories, only those are included here in which the temperature was recorded, in all, 28 reports. The range of the elevation of temperature was between 99 and 104 F, the average being 100. These elevations of temperature were more commonly observed late in the disease, after metastases had occurred, but fever was noted early in the clinical course in 30 per cent of the cases. Associated with this fever, in many cases, was a slight albuminuria and the presence of a few white and red blood cells in the urine. Though a search for Bence-Jones bodies was apparently not a routine procedure, in the cases in which the test for these bodies was carried out, they were not found in a single instance.

In cases in which the blood was examined in detail, the picture ranged from that of the normal type to that of a secondary anemia and from that of relative leukopenia to that of marked leukocytosis. Of thirty-one cases in which complete blood counts were made, five presented red cell counts of 5,000,000 or more and an equal number, red cell counts of 4,000,000 or more. The remaining twenty-one cases showed red cell counts ranging between 2,900,000 and 3,900,000. No case showed anemia of the primary type with high color index or severe secondary anemia. The hemoglobin in these cases ranged between 40 and 90 per cent, in thirteen it was from 80 to 90 per cent, and in eighteen it was from 40 to 79 per cent.

The white cell counts presented no peculiarity. Of thirty-one cases in which the white cell count was recorded, eight had counts within normal limits, twenty had counts of more than 10,000 and three of more than 20,000, the average being 15,200. There were no unusual features in the differential counts, save for an occasional eosinophilia ranging from 4 to 20 per cent in a count of 100 cells. The polymorphonuclear cells rarely showed an increase beyond 70 per cent of the total count, though, in one case, they presented an absolute increase in number to 95 per cent. Myelocytes were not noted nor any increase in the number of the mononuclear elements. Leukocytosis was not restricted to cases with metastases, but was often an initial observation early in the course of the disease.

Of peculiar interest is the great variability in the nutrition of the patients suffering from Ewing's sarcoma. In some cases in the series a noticeable loss of weight over a relatively short period of time was observed early in the course of the disease while in other cases little

or no evidence of undernutrition was seen until the end of the clinical course. The terminal phases of the disease, however, revealed a progressive emaciation in most of the cases observed.

Internal metastases usually presented themselves clinically late in the disease. In many cases, there was pulmonary involvement with pains in the chest, hemoptysis and other clinical manifestations of pulmonary disease. In no case were there primary changes of the lungs due to changes in body stance, as often occurs in multiple myeloma, because in the cases of Ewing's sarcoma the progress of the disease was usually

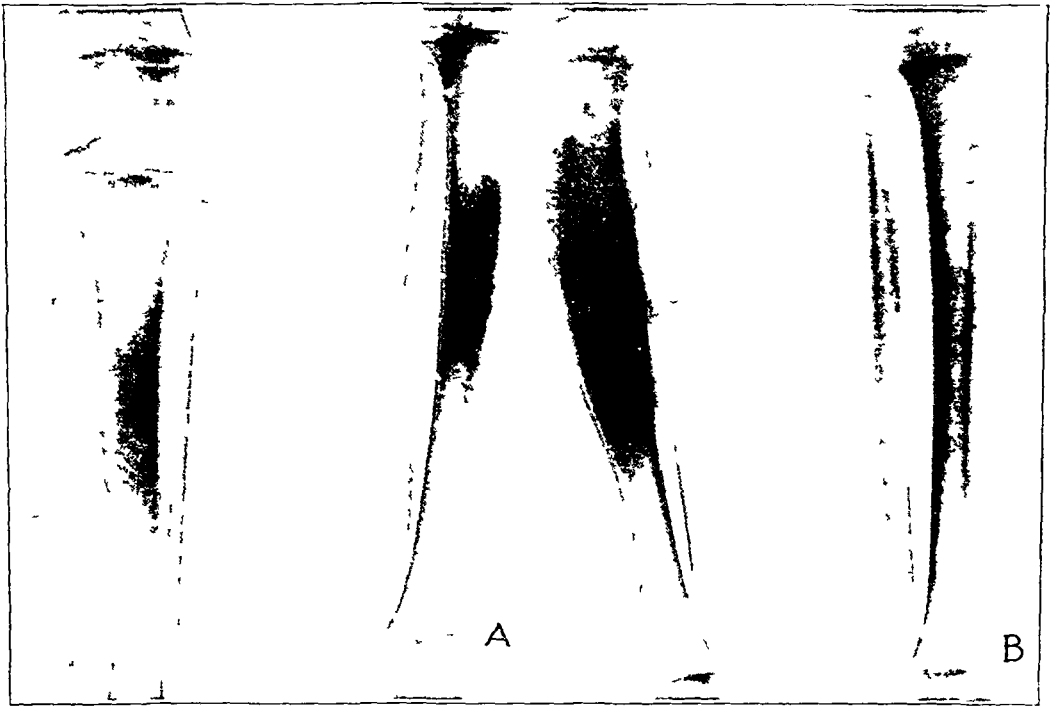


Fig 3—4 is a roentgenogram of a tibia made six months after the onset of symptoms. It shows a slight shadow in the midshaft region of the bone and a slight widening of the cortex, with little if any periosteal reaction. B was made eleven days later. It shows increased density of the tumor shadow and a definite periosteal reaction. The normal tibia is included in B for contrast.

too rapid and vertebral metastases when they occurred were terminal. In one patient showing choked disks and retinitis, blindness developed but this was due to metastatic involvement of the cranial vault with protrusion into the cranial cavity rather than to direct involvement of the brain substance. Not infrequently with metastatic involvement of the skull and vertebrae evidence of motor irritation either of the spinal cord or of the cerebral cortex was expressed in the form of spastic extremities.

Local changes about the tumor were not uncommon, such as dilatation of the veins, hyperemia of the affected part or edema immediately surrounding the area of tumor. Sometimes the entire limb below the site of the lesion was swollen.

#### ROENTGEN-RAY STUDIES ✓

Ewing's sarcoma, as seen by the x-ray, is most often diffuse and situated near the midshaft region of a long bone. The earlier stages of the lesion present the more difficult diagnosis, and the difficulty is enhanced by the variability in the appearance of the bones affected and infiltrated by the tumor. In one case of this series (fig 3 A) an x-ray picture

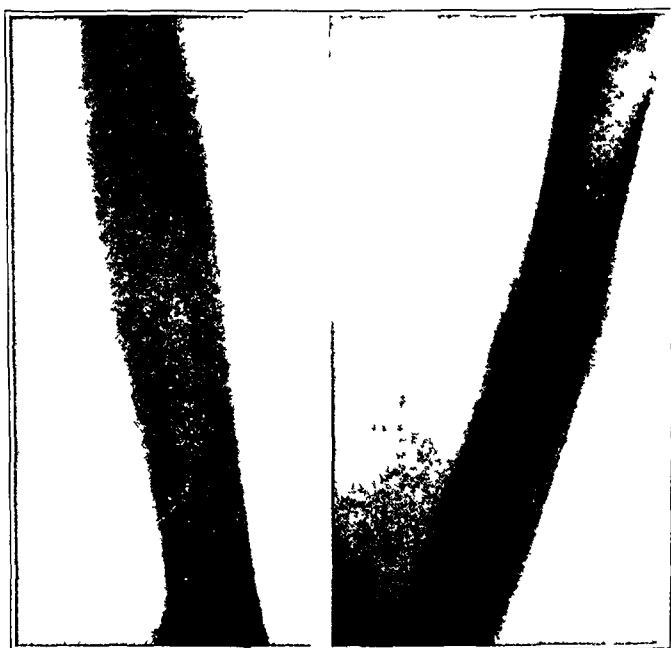


Fig 4—Ewing's sarcoma in an early stage. There is relatively little medullary involvement, a slight expansion of the shaft and thickening of the cortex. There is a periosteal reaction, looking somewhat like onion peel.

was made six months after the onset of symptoms. When studied, it revealed a slight shadow in the midshaft region of the bone and a widened but apparently well preserved cortex, with little or no periosteal reaction. An x-ray picture (fig 3 B) made eleven days later revealed a fully developed Ewing's sarcoma, with increased density of the tumor shadow and definite periosteal reaction.

X-ray pictures were available for study by the authors in twenty-six cases in this series. Of this number six represented early stages which showed relatively little medullary involvement, the duration of symptoms having been from two to seven months (fig 4). The roentgenograms in

these six cases showed a slight expansion of the shaft with a periosteal reaction looking somewhat like onion peel. The cortex of the shaft appeared thickened with some mottling in the region of the medullary cavity, due to areas of increased density. The roentgenograms in the other twenty cases made later in the course of the disease showed a considerable part of the shaft affected, apparently the tumor extended more readily in a plane parallel to the axis of the bone. In the areas thus affected the medullary cavity often showed osteoporosis and the cortex evidence of destruction (fig 5). In all of the cases in this group, there were varying degrees of periosteal reaction besides invasion

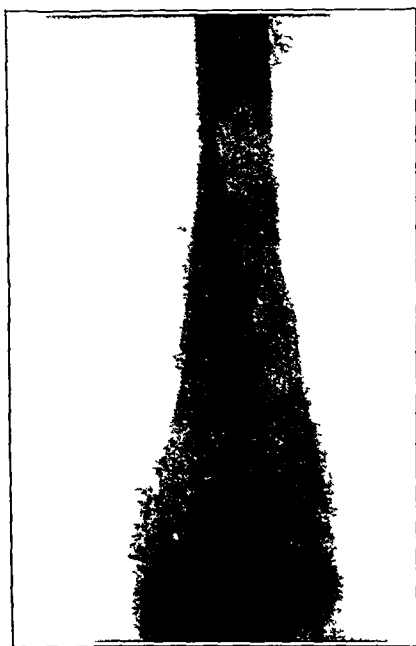


Figure 5

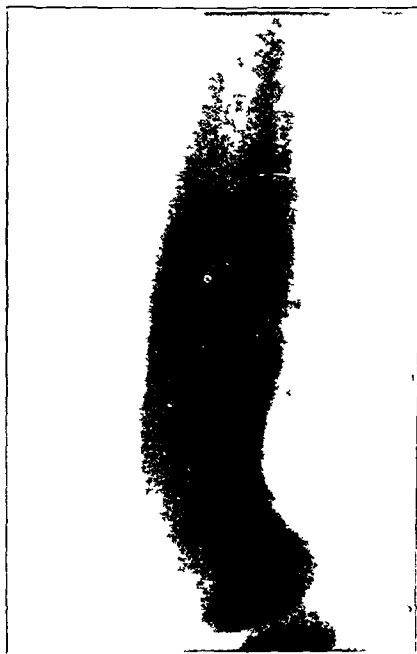


Figure 6

Fig 5—Ewing's sarcoma involving the shaft of a femur (no 27511, tables 2 and 5). One may observe the metaphyseal location of the tumor and the predominant destruction of bone. Such destruction as an outstanding feature was found late in the disease in the majority of the cases.

Fig 6—A roentgenogram of Ewing's sarcoma showing osteophytes at right angles to the cortex, together with a thickening of the cortical bone. This reaction is metaphyseal and diaphyseal (no 22795, table 5).

of the marrow cavity, but the increased density of the bone in the region of the widened cortex was the most characteristic evidence of infiltration by the tumor.

Osteophytes arranged irregularly or at right angles to the cortex (fig 6) appeared in the pictures occasionally. An investigation into

the nature of these osteophytes is of interest and will be presented later in some detail. Suffice it here to say that the perpendicular spicules of bone in Ewing's sarcoma are a normal type of bone formation brought about by a disturbance in the relation of the periosteum to the cortex.

In only two cases did the roentgenogram reveal a suggestive involvement of the epiphysis (fig 7), and in these cases the epiphyses were subsequently proved to be only secondarily invaded, the original tumor having arisen in the shaft of the bone. When the tumor had invaded the muscles, the soft part shadow was often well circumscribed.



Fig 7—Involvement of the epiphysis by Ewing's sarcoma. This was subsequently noted to be a secondary invasion, the original tumor having arisen in the shaft of the bone. Osteophytes may be seen arranged perpendicularly to the cortex, with considerable destruction of cortical bone.

The roentgen-ray observations may be summarized by saying that Ewing's sarcoma expands the shaft of long bones by a diffuse infiltration, which results in a widening and increased density of the cortex and a mottling of the marrow cavity. Both formation of new bone and destruction of bone are secondary to infiltration of bone by tumor. In the early stage, formation of bone predominates, giving rise eventually to either parallel or radiating spicules of new reactive bone. In the later stages destruction of bone, both medullary and cortical, characterizes the x-ray picture.

The x-ray studies do not support the view that Ewing's tumor is primarily a neoplasm destructive of bone, for in six of seven early cases the first evidence of infiltration by the tumor was an increase in the density of the bone. The typical contour of the involved area in the bone is also against the current conception of the medullary origin of

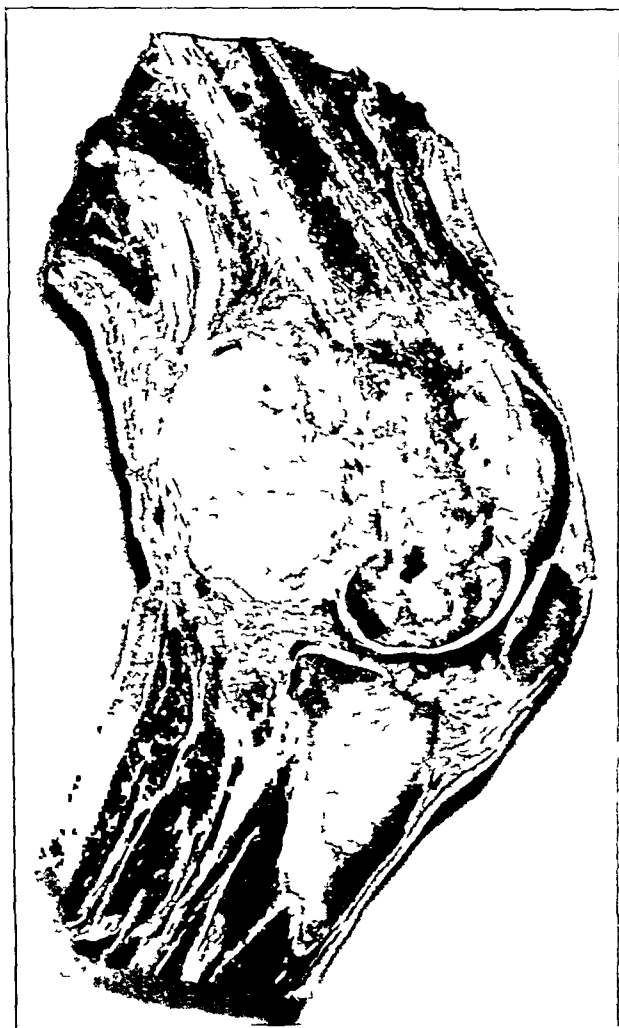


Fig 8—A gross specimen in longitudinal section showing the primary involvement of the shaft with a secondary invasion of the epiphysis. The bulk of the tumor is beneath the periosteum and outside the cortical region. The tumor appears to be well encapsulated (no 26916, tables 2 and 4)

this neoplasm. Medullary tumors should show an approximately spherical shape in the x-ray picture, because their expansion is unhindered in three and usually four directions. In contrast to this the area infiltrated



by the Ewing tumor is generally elliptical, with its long axis parallel to the shaft of the bone, indicating that the growth is resisted in the two opposite directions

#### GROSS OBSERVATIONS

An analysis of the pathologic changes in Ewing's tumor made from gross specimens of bones containing the tumor aided materially in the interpretation of the x-ray pictures. The location was usually the shaft



Fig 9—A gross specimen of a humerus in longitudinal section. The widened cortex described in the x-ray picture is shown, in the gross specimen, to be made up of subperiosteal and endosteal formation of new bone, which encroaches on the medullary space (no 37472, table 4)

of a long bone, and the zone of involvement extended from the midshaft region to the epiphysis, the epiphysis being secondarily involved (fig 8) in but three instances. Regardless of the site of origin of the tumor, all the gross specimens with one exception showed the bulk of the tumor lying subperiosteally (fig 8). The medullary cavity sometimes contained a small portion of the tumor, but usually this region was constricted or totally occluded by new reactive bone (fig 9). The widened

cortex described in the x-ray pictures was shown in the gross specimens to be made up of subperiosteal and endosteal formation of new bone which encroached on the medullary space and frequently sealed it off from invasion by the tumor



Fig 10—A photomicrograph showing the periosteum with its subperiosteal layer forming spicules of reactive bone peripheral to the invasion by tumor. One may note osteoblasts about the spicules of bone. These spicules constitute the right angle formations of bone seen in the x-ray pictures (no 34005 table 5)

Although in one case the shaft of the bone surrounded by tumor was almost destroyed in the majority of the specimens destruction of bone was not a prominent feature. The tumor in its early stages appeared to infiltrate rather than to destroy bone, and the bone thus infiltrated

reacted vigorously with formation of new bone. But the bone subsequently did undergo destruction when surrounded and infiltrated by the tumor, apparently as the result of interruption of the blood supply where the tumor had invaded and blocked the Volkmann and Haversian canals.



Fig 11—A photomicrograph of a cross-section, from the humerus of a human embryo 90 mm long. One may note the enclosure of vessels by osteoid tissue in the cortical region. The vessels remain as units in the future Haversian systems. The cartilage in the center of the bone is being gradually destroyed and replaced by marrow elements.

When the involvement of the bone was diffuse, the subperiosteal formation of new bone was both parallel and at right angles to the cortex (fig 3). As was pointed out by Buerger<sup>16</sup> in a case of "disso-

<sup>16</sup> Buerger L. Bone Sarcoma. Surg Gynec Obst 9:441, 1909, Further Studies of Sarcoma of Bone. Am J M Sc 140:355, 1910.

lutive" sarcoma, this normal formation of new bone was fairly striking in various parts of the tumor. The origin of this bone is explained by the mode of advance of the tumor. Due to the growth of the tumor and subsequent hemorrhage, there is a gradual separation of the periosteum from the underlying cortex. The parallel deposits of new bone appear to be the result of proliferation of the peripheral layer of the



Fig. 12—High magnification of a cross-section of the humerus from a human fetus 2 months old. It shows the invasion of the osteoid rim and endochondrium by a vessel bud from the fetal periosteum preceded by a giant cell. Volkmann's canals are formed about these periosteal vessels and blended with the haversian systems at a later stage.

cortex when the periosteum has suffered minute separation from the bone. This gives the onion peel-like formation characteristic in x-ray pictures of the early stages. With increased separation of the periosteum spicules of new bone from the subperiosteal region are laid down at right angles to the shaft rather than parallel (fig. 10). We agree with Ribbert that this is due to the blood vessels perforating Volkmann's

canals,<sup>17</sup> which determine the direction of the new growth of bone when they are pulled outward in maintaining their continuity after the periosteum has been elevated. The two types of formation of bone, parallel and radiating, duplicate the process observed in the embryo. The bone laid down parallel to the shaft is the first to appear in the tumor and also in the embryo. In the first two months of life, osteoblasts about budding vessels lay down osteoid tissue parallel to these channels, and form



Fig 13—A longitudinal section of a fibula showing involvement by the tumor. Cysts may be seen at the periphery of the tumor, filled with a dark, pigmented, jelly-like material. The bulk of the tumor is subperiosteal in location (no. 34422, tables 2 and 5).

the inner part of the future cortex, the vessels remaining as units in the future haversian system (fig. 11).

About the second month of embryonic life, this thin osteoid rim of bone is perforated by vessels from the fetal periosteum<sup>15</sup> preceded by giant cells (fig. 12). The reformation of bone about these periosteal

17 Stohr, P. Textbook of Histology, Philadelphia: P. Blakiston's Son & Company, 1903, p. 151.

vessels forms the Volkmann's canals seen in the mature bone which unite the periosteal blood supply with the haversian vessels. This determination of the pattern of the bone by vessel units typical of the embryo<sup>18</sup> is not lost in adulthood.

The soft part tumor formation was usually encapsulated by a thin layer of fibrous tissue which at its margin was continuous with the

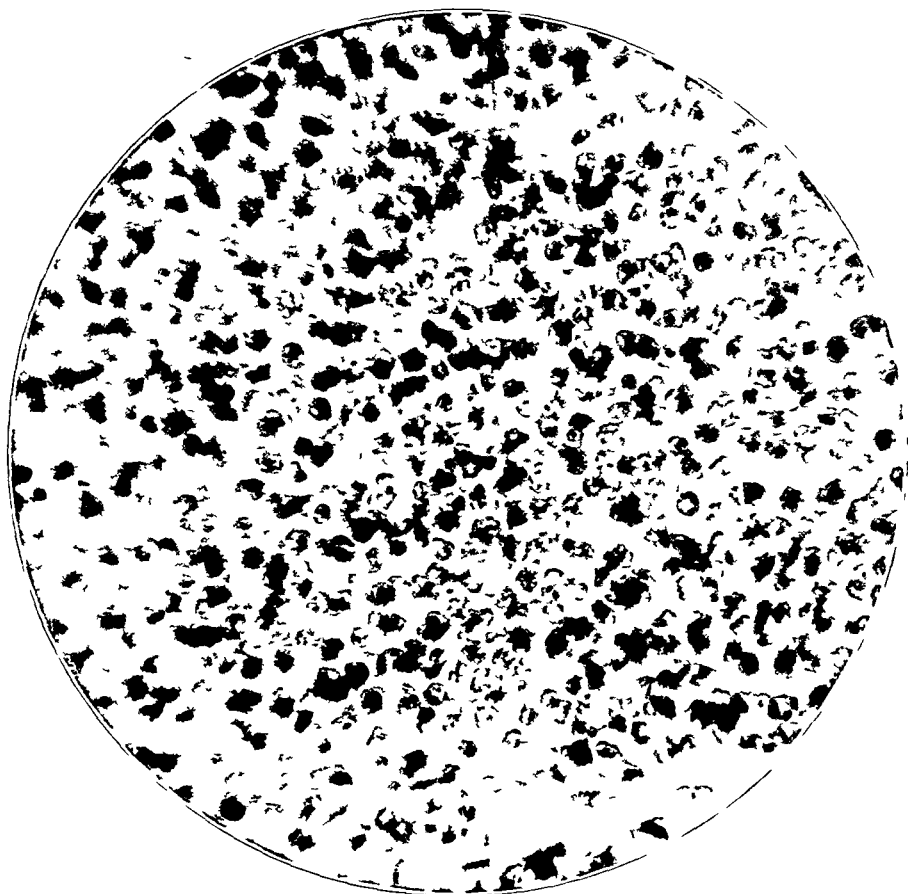


Fig. 14—A photomicrograph showing the characteristic cell of Ewing's sarcoma. One may note the indistinct cytoplasm and the round and oval nuclei (no. 27039, table 4).

periosteum. The tumor tissue itself, enclosed by this capsule, was firm and grayish-white and was divided into characteristic lobules by a number of connective tissue strands extending from the outer capsule to the region of the cortical bone. Occasionally the tumor substance showed cysts (fig. 13) at the periphery of the tumor, filled with a dark

<sup>18</sup> Ewing, E. H. Bone Formation in Osteogenic Sarcoma. *Arch. Surg.* **12**: 867 (April) 1926.

pigmented, jelly-like material. These cysts were due to hemorrhage or regressive changes, for many of the specimens showed soft necrotic areas honeycombing their structure.

#### MICROSCOPIC OBSERVATIONS

The data at hand indicate that the microscopic characteristics of Ewing's tumor are among the most uniform characteristics of the dis-

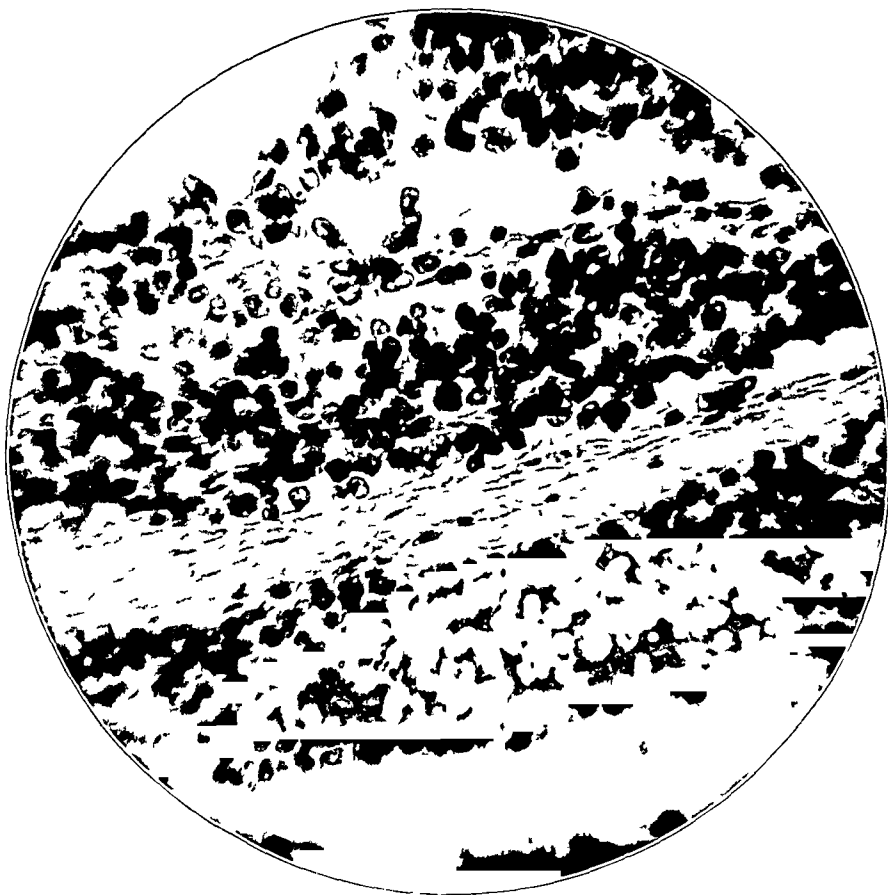


Fig. 15—A photomicrograph showing the uniformity in the size of the cells. In the less compact region, the definite but irregular outline of the cytoplasm may be noted (no. 24667, tables 2 and 4), a septum is seen traversing the tumor substance.

case, and thus are a most important aid to the clinician or the surgeon in making the diagnosis. Examination of sections from these tumors without consideration of special areas, which will be considered later, revealed a more or less constant cellular picture. The type of cell in the compact areas was small and polyhedral with a round or oval nucleus (fig. 14). The cytoplasm was scanty and practically stainless.

In less compact regions, the cells showed a cytoplasm with a more definite outline which surrounded the nucleus with a pale eosin-staining

substance, the periphery of which was irregular (fig 15). The cells were at times so closely packed that the shape of the individual cell was altered. The nucleus was deeply stained, showing a definite limiting membrane and a sparse scattering of chromatin granules without any definite arrangement. Nucleoli were rarely seen, but mitotic figures were noted not infrequently. The diameters of the nuclei ranged from 7 to 9 microns. Little pleomorphism was observed and multinucleated cells of tumor origin were not noted. Not infrequently, however, osteoclasts were located in the region of dead bone or a slight distance from the bony tissue in the midst of tumor cells.

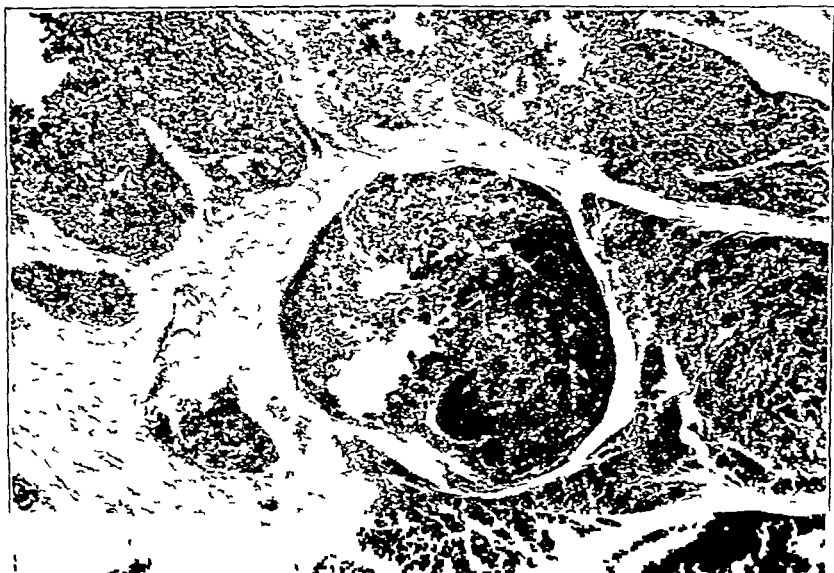


Fig 16—The formation of septums in Ewing's sarcoma giving it an alveolar arrangement (no 24667, tables 2 and 4)

There appeared to be no intercellular stroma, but a fibrous trabeculation with a hyaline-staining intercellular substance divided the tumor tissue into lobules where it infiltrated the soft parts. These septum formations often gave the tumor an alveolar arrangement (fig 16).

Vascularity was a variable feature of these tumors, in some it was marked (fig 17). In certain sections taken through areas of bone haversian canals occupied by blood vessels were secondarily infiltrated by tumor cells (fig 18). In these localities the tumor cells were sometimes within and sometimes without the vessel walls. Phenomena of this character have been cited by some authors as evidence of the seat of origin of Ewing's sarcoma. We are inclined to the belief, however, that in most of these instances tumor cells were traversing the haversian system following the path of least resistance in their invasion of bone.



Areas of osteitis fibrosa,<sup>16</sup> either subperiosteal or endosteal in origin, were seen where the tumor was invading bone. Here osteoid spicules were found, surrounded by osteoblasts and fibrous tissue (fig 19), the new bone thus formed being typical of the process described by us as occurring in bone cysts and giant cell tumors. This reaction, we believe, is an attempt by the bone to heal itself, in a manner often noted in fractures, by a metaplasia of fibroblasts to osteoblasts and to osteoid tissue.



Fig 17—A photomicrograph showing blood vessels surrounded by tumor and the infiltration of tumor by hemorrhage. One may note the marked difference between the tumor cells and the cellular elements comprising the blood vessels (no 35654, table 5).

In some sections, islands of tumor cells with a blood vessel at the center were surrounded by areas of necrosis, the blood supply apparently being inadequate for more than the tumor cells immediately surrounding the vessel. Such necrotic areas were referred to by Kolodny as hydropic degeneration of tumor cells and by other authors as a peritheliomatous structure.

The periphery of the tumor in many cases was infiltrated by cells of the polymorphonuclear or monocytic types. This infiltration by round cells was most common in the cases of longer duration or in those in which the tumor had previously been explored, and not infrequently had led to an erroneous diagnosis of osteomyelitis at biopsy. Eosinophils were frequently observed along with the round cell infiltration, both of these processes indicating, in all probability, a response to chronic irritation. An infiltration by plasma-like cells was noted in only



Fig 18—Note the invasion of haversian canals by tumor. The tumor is extending along the vessel in one haversian canal, while other canals are completely filled with tumor cells.

nine cases of the series. This, possibly, had no special relation to the tumor, as sections of normal bone sometimes show such cells. On finding these cells, certain authors have suggested a relation between this tumor and multiple myeloma.

A peculiar type of cell about the same size as the Ewing sarcoma cell was often observed in these tumors. It contained a small deeply-staining nucleus eccentrically placed and a clear eosin-staining cyto-

plasm The locality in which these cells were found related them to the haversian canals, and in such conditions as bursitis we noted them proliferating about the blood vessels in the haversian systems

#### DISSEMINATION AND METASTASES

True to the nature of malignant disease, dissemination has occurred in every case of the series which to the time of writing has terminated in

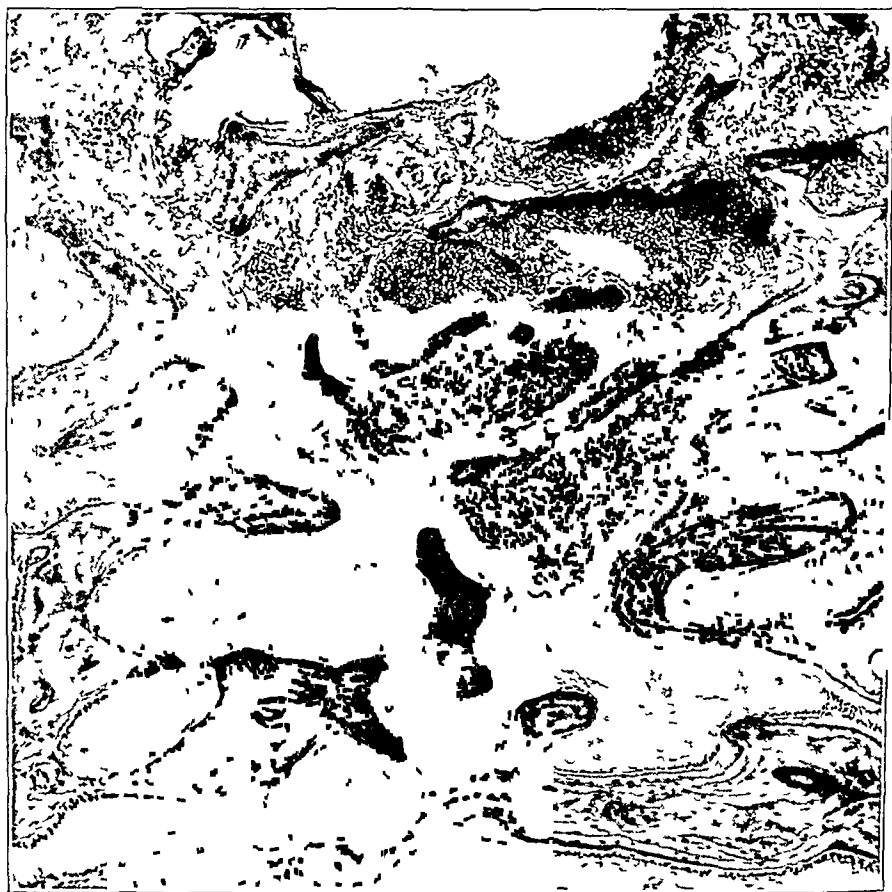


Fig 19—A photomicrograph showing osteitis fibrosa surrounding the invading tumor The osteoid spicules are surrounded by osteoblasts and fibrous tissue (no 15745, table 5) This osteoid reaction represents the reparative nature of all bone, no matter what the source of the injury

death The extent of metastases has been most difficult to localize because of the insufficient data included in many of the case reports, necropsy having been relatively rare in the series Only those cases in which definite proof of metastases was obtained either by x-ray, biopsy or necropsy are included here, though death in every case was said to have been from tumor

The most frequent sites of metastases were the lungs the lymph glands and the skull (see table 2 and fig 20) The most unique feature in the dissemination was the predilection of the secondary growths for other bones Although some observers view this dissemination to other bones as proof that the tumor is primarily a multiple disease of the skeleton in our series it was nearly always possible to obtain a definite latent period of from two and a half months to a year between the initial appearance of the tumor in a single bone and its involvement of other bones

TABLE 2—*Primary Lesions with Metastases*

Patient* (Surg Path Lab No)	Original Location of Tumor	Duration of Symptoms at Time of First Observation Months	Location of Metastases	Duration of Life Following Treatment Months
40530	Tibia, lower shaft	4	Skull femurs lungs humeri scapulae	(Living after 9 mo)
34422	Tibia upper shaft	4	Internal organs	5 <sup>2</sup>
34344	Femur lower shaft	5	Humerus	20
32623	Radius lower shaft	5	Lungs	17
31175	Fibula midshaft		Lungs	16
30944	Tibia lower shaft	7	Scapula clavicle	5
30755	Fibula upper shaft	2	Lungs	10
29054	Tibia midshaft		Skull	22
28835	Femur lower shaft	4 <sup>1</sup> / <sub>2</sub>	Lungs	4 <sup>1</sup> / <sub>2</sub>
28774	Ilium	5	Skull	(Died at operation)
28600	Humerus upper shaft	1 <sup>1</sup> / <sub>4</sub>	Lungs	15
28364	Fibula upper shaft	2	Lungs ribs skull	6 <sup>1</sup> / <sub>2</sub>
27511	Femur lower shaft	6	Lungs skull spine	5
26916	Femur	11	Ribs 2 vertebra 1 thrombosis iliac vein	12
26597	Os calcis	24	Lungs	6
25900	Scapula	24	Gland- spine	14
25430	Fibula midshaft	12	Glands	13
24667	Femur upper shaft	14	Spine	15
15921	Pelvis		Glands	
13439	Humerus mid-shaft	5	Glands	14
10537	Tibia upper shaft	6	Skull	9
5172	Fibula upper shaft		Skull glands	2
4392	Humerus upper shaft	3	Glands internal organs	9
3009	Femur upper shaft	36	Internal organs	
1207	Fibula upper shaft	9	Vertebrae	9
64	Humerus upper shaft	6	Gland- internal organs	5

\* The patients were proved to have metastases by x-ray biopsy or necropsy

The bones most frequently involved by metastases were the skull, the spine and the scapula or the clavicle although dissemination to the long pipe bones also occurred This is well illustrated by the case of a white boy aged 14, examined in this clinic and later operated on in a neighboring city This patient, although still alive at the time of writing, has extensive metastases to the skull, the femora the humeri and the scapulae The lungs are involved, and he has also become blind the left eye protruding markedly from its socket When he was first observed only the tibia was affected

Enlargement of the lymph nodes was reported in fifteen cases and in seven cases involvement of the glands was proved by microscopic examination The lungs were demonstrated to be the seat of metastases in thirteen instances in many others pulmonary involvement was evi-

denced by hemoptyses pain in the chest or a high terminal fever. In four cases, metastases to internal organs were noted without reference to the specific organs involved.

In the clinical picture of Ewing's tumor, the involvement of a single bone early in the disease with later dissemination of the neoplasm to other bones constitutes a unique and important feature setting this tumor apart from other tumors of the bone. In contrast to multiple myeloma or chloroma, it is unusual for the patient to present himself for examination with more than one bone involved, and in such a case, a single focus usually predominates in size, as well as in duration of growth.

CASES	SITES OF METASTASES							
15								
10								
5	LUNGS							
0		SKULL	GLANDS	INTERNAL	SPINE	LONG BONES	SCAPULA	RIBS & CLAVICLE

Fig. 20—Sites of metastases in cases of Ewing's sarcoma. The column to the left shows the number of cases.

#### CLINICAL COURSE

In order to correlate the early clinical observations with the subsequent course of the disease, a brief turn will be made in survey of the more characteristic features of Ewing's sarcoma, emphasizing the typical course of the disease.

At the onset of Ewing's tumor most often there is tenderness or soreness of the affected part followed by pain of either a dull aching or a sharp shooting quality. The patient's attention is first called to the malady by trauma, spontaneous pain or pain with formation of tumor.

From this initial phase, the patients pass on to a period marked by more continuous pain and often the nocturnal pain may be the most severe. The intervals of freedom from such attacks of pain become less and less. In many instances, the tumors have a tendency to regress

for a time leading the patients to think that a cure has been effected only to recur again, becoming larger in size and accompanied with more severe pain

The formation of the tumor is often accompanied by some constitutional reaction, expressed in an elevation of temperature to 100 F on the average and with localized redness and swelling of the subcutaneous tissue or dilatation of the peripheral veins

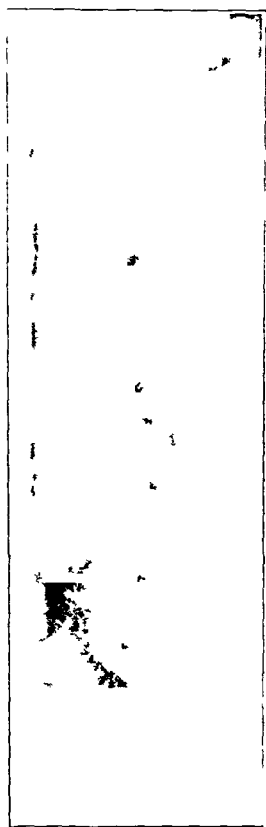


Fig 21—A case of Ewing's sarcoma in the femur which is not unlike the early stage of inflammatory disease of bone

On examination a tumor is usually palpated which varies from a small localized swelling in some cases to a large fusiform mass in others and which is apparently continuous with the sheath of the bone. The soft parts over the tumor in most cases are freely movable although they may be somewhat edematous and inflamed. The majority of the cases presented an indurated mass not however of bony density with occasional slight crepitus due to the osteophytes in the tumor or the soft parts

The x-ray examination usually reveals a diffuse lesion on the shaft side of a long bone. The involved region is widened by periosteal and endosteal formation of new bone, and there may be considerable subperiosteal tumor. The marrow cavity is either narrowed or mottled by reactive bone, and occasionally one sees in a subperiosteal tumor spicules of new bone at right angles to the cortex, although the usual picture is a laminated formation of bone extending along the shaft in parallel

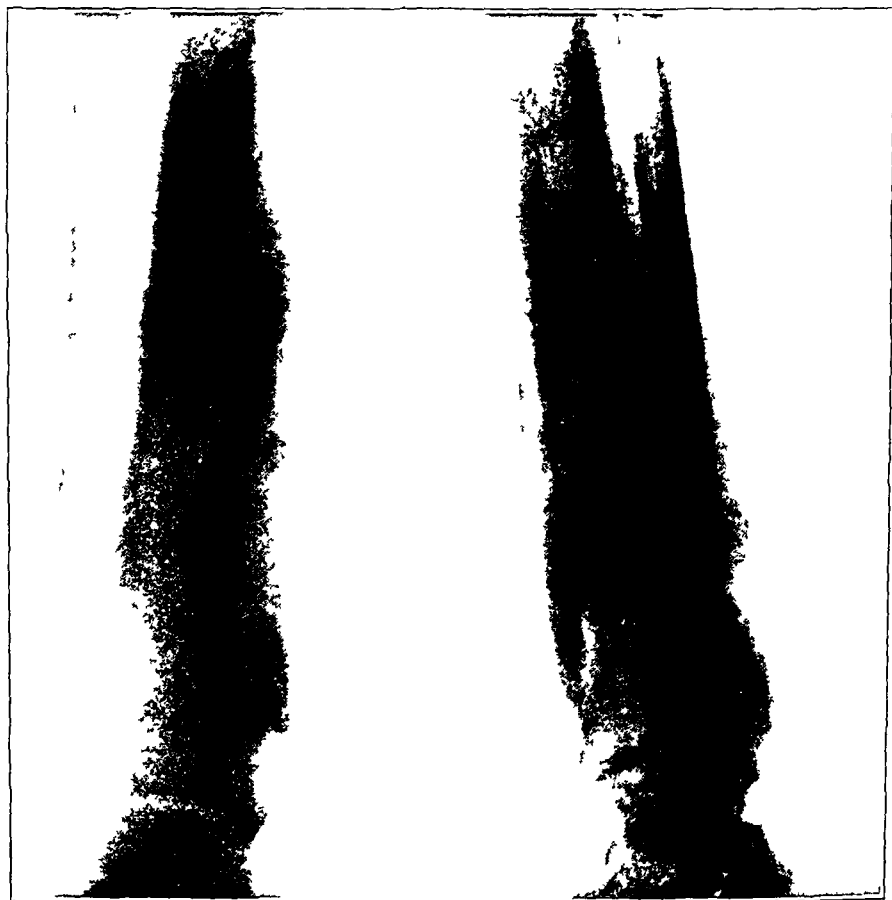


Fig. 22—Pyogenic osteomyelitis involving the lower end of a tibia. The involucrum is distinct and the shaggy periostitis is a noteworthy diagnostic point.

fashion. In no case is the epiphysis primarily involved, although in late lesions it may be secondarily affected, with evidence in the shaft above of destruction of bone in the medullary and cortical regions.

The red cell count ranges from a normal count to that of a moderate secondary anemia with or without leukocytosis. The average leukocyte count is 15,000. The differential count, in the majority of instances, is within normal limits.

In many cases the patient gives a history of normal activity for a year or more before being confined to bed. Pathologic fracture is extremely rare. It was noted only three times in this study.

In two thirds of the cases the course of the patient's health was downward although temporary relief was obtained by operative proce-



Fig. 23—A low-power photomicrograph showing osteomyelitis of bone with a healing bone reaction surrounding fibrous tissue. An x-ray picture of the same case is shown in figure 24.

dures. The usual termination is with metastases, but the time of their appearance is difficult to determine accurately because of the paucity of clinical data covering this point.

Loss of weight and secondary growths in other bones, often in the skull and the spine, are frequently seen late in the disease, with an occa-



sional paraplegia. Hemoptyses, thoracic pain and fever are terminal manifestations. In eight cases in this series life was greatly prolonged and an apparent cure effected by radical operation and irradiation, the length of life, at the time of writing, having been from twenty months to nine years after operation.



Fig. 24—Chronic sclerosing osteomyelitis. There is a periosteal reaction above the metaphysis. As nothing in the history helped toward a diagnosis, an exploration was necessary to rule out sarcoma. A photomicrograph is shown in figure 23.

#### DIFFERENTIAL DIAGNOSIS



Many patients with disease of the bone are now coming under observation at a relatively early stage of their disease, thus making the differential diagnosis, especially by x-ray, more difficult and more important. A careful survey of the clinical history with every available laboratory procedure is often necessary to differentiate Ewing's sarcoma from other lesions of bone.

Among the many diagnoses first made and later revised in cases of Ewing's tumor filed in the Surgical Pathological Laboratory it is interesting to note that the diagnosis of inflammatory disease of the bone predominates. A primary diagnosis of pyogenic periostitis or osteomyelitis<sup>19</sup> was made in ten cases, tuberculosis of the bone in nine cases<sup>20</sup> syphilitic periostitis or osteomyelitis in six cases<sup>21</sup> and typhoid osteomyelitis in one case, thus showing the frequency with which Ewing's tumor is confused with chronic inflammation of the bone.

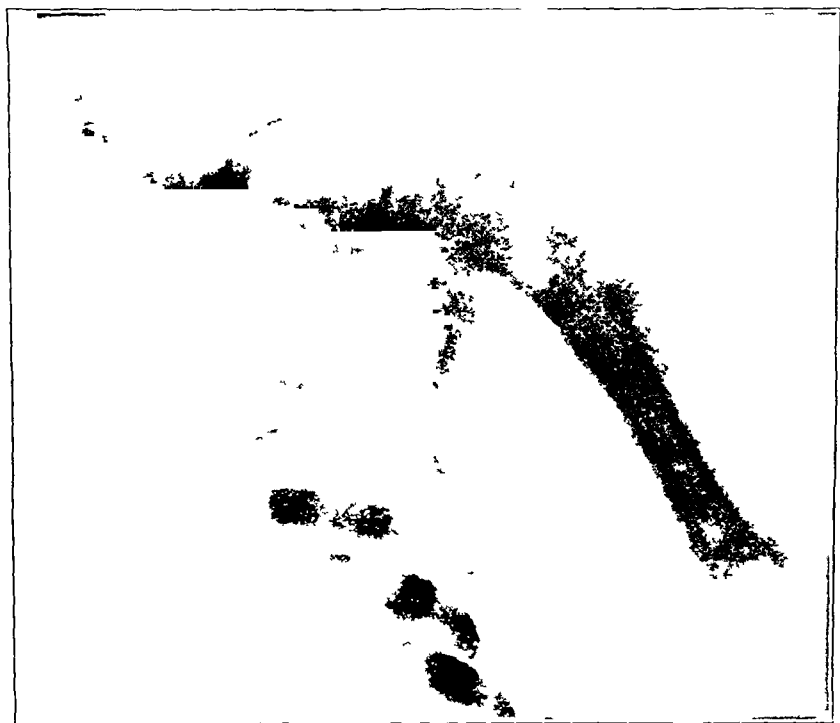


Fig. 25—A tuberculous humerus showing marked destruction in the epiphyseal end of the bone, with involvement of the joint.

Often the intermittent pain, in many cases following trauma in other cases occurring spontaneously with some constitutional response, makes for a diagnosis of osteomyelitis. The roentgenogram may not be unlike that of inflammatory disease of the bone (fig. 21), and the biopsy may further substantiate the diagnosis, the surgeon not having gone deep

19 Bloodgood, J. C. A Brief Summary of Benign and Malignant Lesions of Bone. *Southern M. J.* **19**: 541, 1926.

20 Knapp, R. L. The Inflammatory and Toxic Diseases of Bone. New York: William Wood & Company, 1926, p. 57.

21 Bloodgood, J. C. Differential Diagnosis of Periosteal Lesions. *Radiology* **3**: 432, 1924.

enough to reach intact tumor cells but having removed only a peripheral portion of the tumor infiltrated with mononuclear cells and some fibrous tissue

Ewing's sarcoma is more often confused with subacute and chronic pyogenic osteomyelitis than with the acute form. As was pointed out by Starr,<sup>22</sup> the acute form of osteomyelitis, in the majority of instances, occurs between the ages of 2 and 10, and because of its sudden onset with malaise, nausea, high fever, rigors, localized boring pain and a leukocyte count of from 25,000 to 30,000, should not often be confused with Ewing's tumor, especially when a primary focus of infection can be demonstrated.

The chronic forms of osteomyelitis commonly show suppuration, except sclerosing osteomyelitis (Garie's type), which shows suppuration in about 10 per cent of the cases,<sup>23</sup> whereas Ewing's sarcoma shows this only in the extreme case or after a previous operation. In the roent-

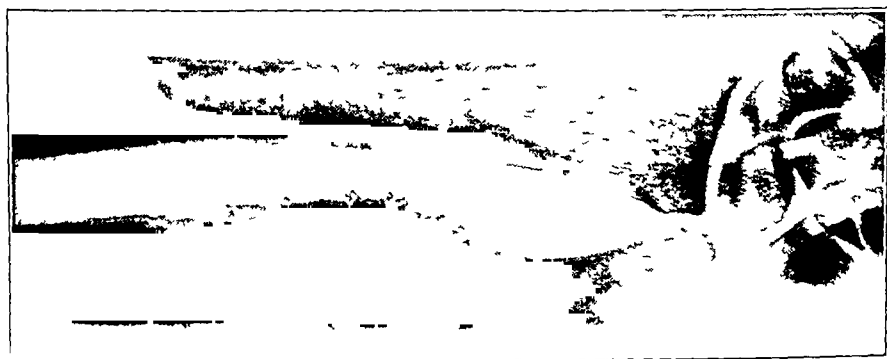


Fig 26—A syphilitic lesion in the shaft of an ulna. There is considerable formation of bone beneath the periosteum. Osteophytes extend at right angles to the cortex inwardly from the periosteal region. Similar reactions are seen in malignant tumors of bone.

genogram of osteomyelitis an involucrum is commonly seen, but practically never appears in the roentgenogram of Ewing's tumor. This, together with the usual shaggy periostitis and varying degrees of definite destruction of bone (fig 22), is a noteworthy diagnostic point in chronic osteomyelitis. Biopsy shows the characteristic infected tissue with healing bone surrounding a fibrous zone (figs 23 and 24).

Tuberculosis of the bone,<sup>24</sup> in contradistinction to Ewing's sarcoma, is most frequent about the upper part of the femur, though it often

22 Starr: Osteomyelitis, in Lewis: Practice of Surgery, Hagerstown, Md, W. F. Prior Company, 1927, vol 2, p 4.

23 Bloodgood, J. C.: J. Radiol. 1: 147, 1920.

24 Coley, W. B.: The Differential Diagnosis of Sarcoma of the Long Bones, J. Bone & Joint Surg. 10: 420, 1928.

occurs in other locations. The age does not help in diagnosis of tuberculous disease of the bone, but the underdeveloped and undernourished condition of the patient and the slow progress and lack of severity of the symptoms together with the longer period of activity are salient features. The pain in tuberculosis of the bone may be completely relieved by immobilization in contrast with the increasingly severe pains without relief in Ewing's sarcoma. The x-ray picture of a tuberculous bone usually shows marked destruction in the epiphyseal end of a bone with

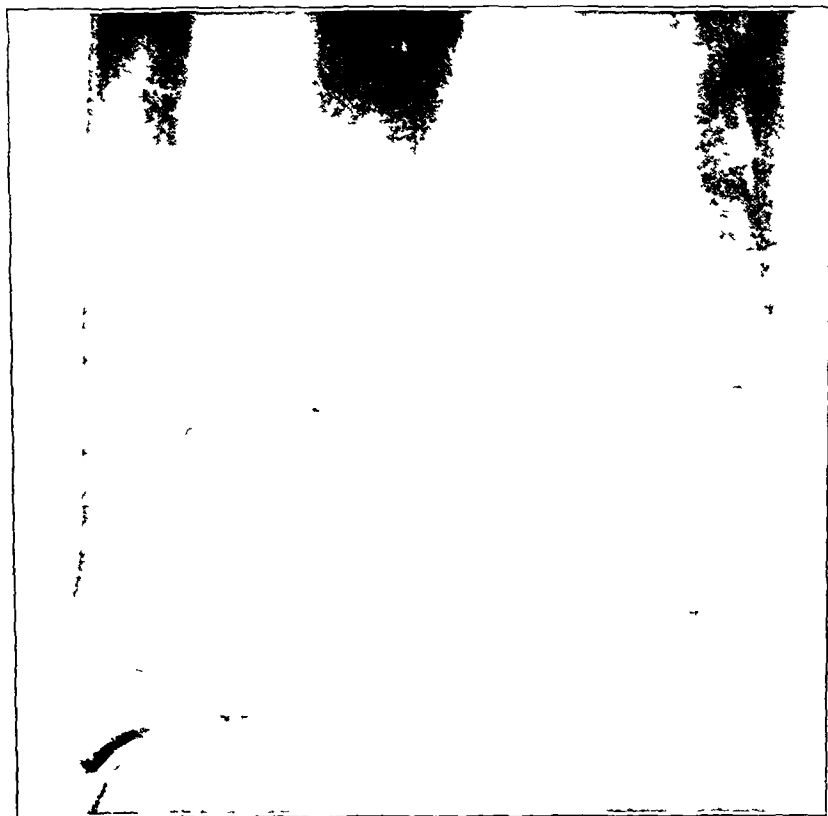


Fig. 27—A syphilitic lesion in the shaft of an ulna showing destruction of bone with little formation of bone. The usual reaction in this disease, however, is an increase in the density of the bone with formation, in many instances of exostoses.

involvement of the joint and calcification of the soft parts (fig. 25). These are rarely seen in Ewing's tumor which practically never shows the sequestrums and draining sinuses observed in tuberculosis.

Syphilitic disease of the bone with which Ewing's sarcoma is often confused, is more likely to occur in later life. The constitutional reaction may not be unlike that of the small round cell sarcoma. Syphilitic

periostitis affects particularly the superficial bones <sup>25</sup> (tibia, clavicle, sternum, ulna, etc.), and usually there is multiple involvement. The periosteum may be bulged, and a formation of small bony spicules, arranged perpendicularly to the cortex of the bone, may occur (fig 26). Kolodny <sup>12</sup> and Eising <sup>18</sup> pointed out that this perpendicular arrangement of osteophytes is sometimes found in low grade chronic infections of bone, pyogenic or tuberculous. This observation is noteworthy, for radiating spicules perpendicular to the cortex in a bony lesion are com-

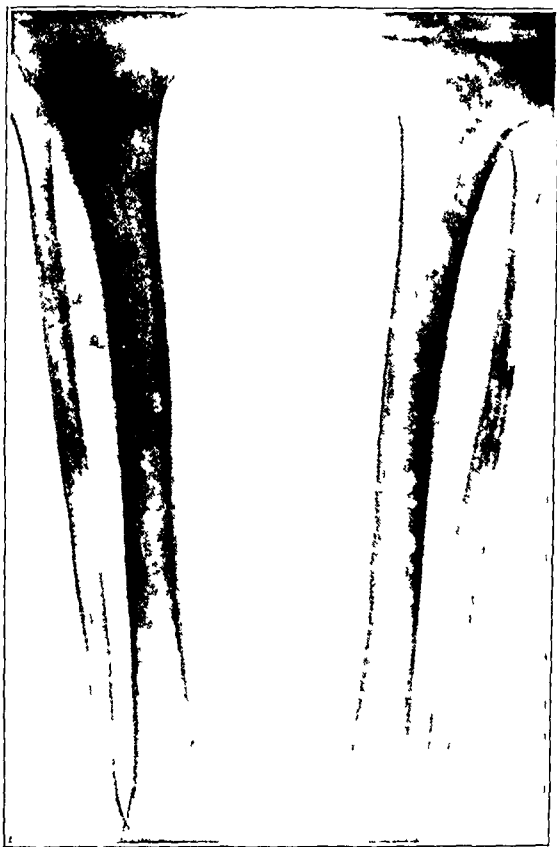


Fig 28—A case of multiple myeloma of the tibia and fibula showing typical punched-out areas. The other bones involved in this case were the spine, sacrum, skull and many of the long pipe bones.

monly associated with a malignant process of bone, Ewing's tumor being no exception. The cortex in syphilitic disease of the bone may be eroded, and medullary destruction may occur (fig 27), but exostoses and increased density of the bone are more constant observations. The Wassermann reaction is therefore all important in the differential diag-

<sup>25</sup> Chenelet, E. Sur les gommes syphilitiques simulant des sarcomes, Thèse de Lyon, 1910. Stokes, J. H. Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1927, p. 685.

nosis and, as was pointed out by Bloodgood<sup>21</sup> and others when a positive Wassermann reaction is present a therapeutic test should be carried out before the tumor is explored

Clinically, multiple myeloma was noted as a source of confusion in two of these cases of Ewing's sarcoma. In a recent publication,<sup>15</sup> we pointed out that multiple myeloma occurs for the most part in persons between the ages of 40 and 70. This is in contradistinction to the age incidence in Ewing's sarcoma, which ranges between the ages of 6 and 20. Multiplicity of tumor was an outstanding feature in over 90 per cent of the cases of myeloma including involvement of the thoracic cage, skeletal deformity occurred in 60 per cent, and pathologic fracture in 63 per cent of the cases. Bence-Jones bodies were excreted in 65 per cent of the cases. In Ewing's tumor, multiple involvement is rarely seen when the patient first comes under observation, fractures occurred in

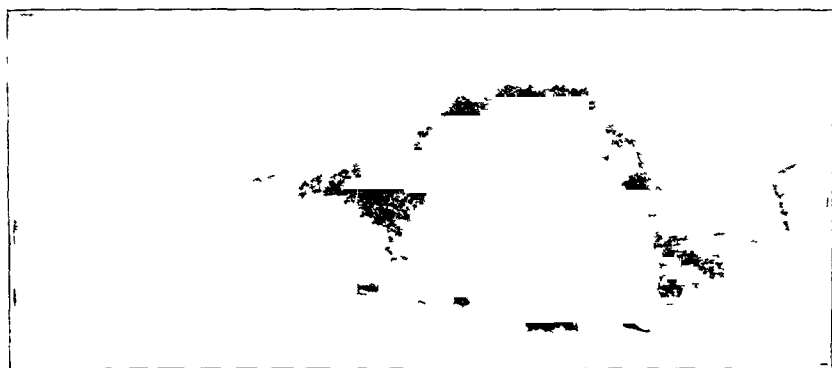


Fig 29—An osteogenic sarcoma involving the lower end of a femur. There is formation of new bone in the periosteal region, with osteophytes arranged both irregularly and at right angles to the cortex. This type of invasion practically never gives the extensive laminated new bone paralleling the shaft seen in Ewing's sarcoma. The medullary cavity is encroached on by sclerosing tumor.

only 5 per cent of the cases, and Bence-Jones bodies were never found in the urine. The X-ray picture rarely showed the multiple, punched-out areas seen in multiple myeloma (fig 28).

The osteogenic sarcoma<sup>26</sup> in the average case is located at the end of the long bone whereas Ewing's sarcoma appears in the shaft and does not involve the epiphysis. The formation of new bone in osteogenic sarcoma shows right-angled spicules early in the disease and practically never gives the extensive laminated new bone paralleling the shaft seen in Ewing's sarcoma (fig 29). There is an occasional exception in osteogenic sarcoma in which there is involvement of the shaft

26 Nicholas B. H. Roentgen Diagnosis of the More Important Tumors of the Long Bones. Surg. Gynec. Obst. **35**: 301, 1922.

with little formation of bone (fig 30) Irradiation of the tumor offers a good therapeutic test The Ewing tumor responds promptly to irradiation, whereas osteogenic sarcoma is little affected

Metastatic carcinoma<sup>27</sup> is not infrequently confused with Ewing's sarcoma, both clinically and in some cases microscopically Carcinoma occurs later in life than Ewing's tumor, the majority of metastatic tumors in bone appearing after the age of 45 A thorough survey of the body for a primary focus often reveals the source of the metastases, thus ruling out Ewing's tumor An x-ray picture of a metastatic carcinoma in bone usually shows a single medullary lesion

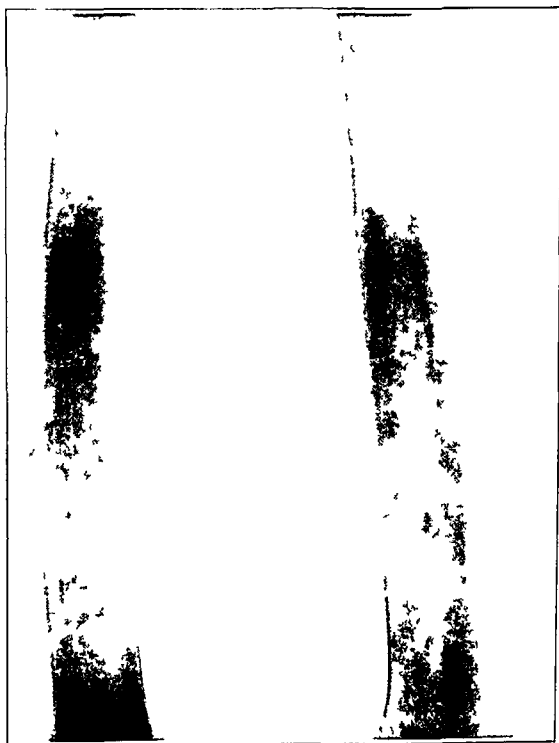


Fig 30—An osteogenic sarcoma involving the shaft of a femur with destruction of bone and some new formation of bone There is considerable periosteal reaction This may be contrasted with figure 29, showing a common type of osteogenic sarcoma found near the end of long bones, which is sclerosing in nature

destroying the bone at the site of the nutrient artery Formation of bone of the healing type is observed in metastatic tumors from the prostate, etc<sup>28</sup> Kaufmann,<sup>29</sup> in a statistical study, pointed out such a

27 Joll, C A Metastatic Tumors of Bone, *Brit J Surg* **11** 38, 1923

28 Simpson W M Diffuse Vertebral Metastasis of Prostatic Carcinoma Without Bony Changes *Am J Roentgenol* **15** 534, 1926

29 Kaufmann E *Lehrbuch der Pathologie*, Berlin, G Reimer, 1911, vol 2, p 759

variation in this type of tumor and the work of Simpson<sup>30</sup> enabled us to make a complete study of metastases to bone. The frequency of metastases to bone in cases of carcinoma is set forth in table 3.

Sacro-iliac strain and rheumatism were also noted as mistaken diagnoses in our series. An x-ray picture usually reveals the true status of the lesion.

#### TREATMENT AND PROGNOSIS

The treatment, as outlined here, is based on the observations of Bloodgood<sup>31</sup> and further supported by the analysis of the cases presented here.

In cases in which metastases have not occurred, amputation for lesions of the lower extremity below the upper third of the tibia and resection of bones for lesions in the upper extremity followed by post-operative irradiation, offer more hope of cure than does irradiation alone. It was recently pointed out that such is the case in all diffuse and periosteal malignant lesions of bone.

TABLE 3—*Frequency of Metastases to Bone in Carcinoma*

Type of Carcinoma	Cases	Percentage Showing Bony Metastasis
Prostate	24	66.0
Hypernephroma	14	56.0
Breast (in Gross cited by Neal and Robnett Arch Surg 14:329 [Feb.] 1927)	423	20.5
Rectum	57	10.5
Esophagus	101	6.9
Thyroid	55	5.4
Uterus	159	3.0
Stomach	309	2.5

If the lesion occurs in the upper part of the tibia or has become so extensive in the upper extremity that the operation of choice is not warranted, irradiation should be resorted to and continued in therapeutic doses until amputation becomes a necessity to relieve pain.

When the lesion is considered operable and the clinical picture, roentgenogram and other laboratory observations are such that sarcoma cannot be ruled out, immediate operation is advised if a competent pathologist is at hand. Never perform a biopsy and wait for a diagnosis from other laboratories. If in doubt take an x-ray, put the affected part at rest and send the x-ray picture and the history of the case to a competent authority for interpretation. The object of the operation is to explore and to get a piece of tissue for frozen section<sup>32</sup> (neutralized

30 Simpson W M Primary Thyroid Carcinoma Simulating Hypernephroma Ann Clin Med 4:668 1926

31 Bloodgood J C Bone Sarcoma Periosteal and Diffuse Type and Their Diagnosis from Benign Lesions J Bone & Joint Surg 8:727 1926

32 Terry B T A Rapid Method of Examining Tissue Microscopically for Malignancy Preparation of Polychrome Methylene Blue J Path & Bact 30:573 1927



polychrome methylene blue stain is used in this laboratory) If the lesion is malignant, the operation of choice based on the site of the lesion must be performed immediately to preserve the life of the patient

The responsibilities of physicians are steadily increasing, as more and more patients come earlier for diagnosis, making the x-ray picture, the gross appearance and the frozen section more difficult to diagnose. Complete studies with careful follow-ups are the ultimate solution of problems in diagnosis of early bone lesions.

At present, we have complete follow-up reports on fifty-two cases of Ewing's sarcoma. In forty-three cases the patients are dead and in eight cases (18 per cent) the patients are living and apparently well at the time of writing. Every patient who is reported well in this series

TABLE 4—*Treatment by Resection or Amputation with Irradiation*

Patient* (Surg Path No.)	Lab	Color	Sex	Age	Location of Tumor	Duration of Symptoms at Time of Operation, Months	Microscopic Observations	Duration of Life Following Operation, Months
37472	W	M	28		Humerus, midshaft	36	Typical	(Well after 35 months)
35882	W	F	6		Tibia, midshaft	6	Typical	26
32623	W	M	11		Radius, midshaft	5	Typical	17
32770	W	M	7½		Tibia, midshaft	18	Typical	16
31775	W	M	22		Fibula, midshaft		Typical	16
28600	W	M	11		Humerus, upper shaft	1	Typical	15
27631	W	F	11		Scapula, clavicle		Typical	(Well after 84 months)
27039	W	M	9		Scapula only	6	Typical	9
26916	W	M	23		Femur, lower shaft	11	Typical	12
26901	W	M	13		Clavicle only		Typical	(Well after 84 months)
25906	W	F	19		Scapula only	21	Typical	11
25430	W	F	10		Fibula, midshaft	12	Typical	18
24667	W	M	11		Femur, upper shaft	11	Typical	18

\* There are three patients (23 per cent) in this group well, with an average duration of life of five years and seven months following treatment. Of this number two are living over five years.

has a duration of life of more than five years since the onset of symptoms, and six are living over five years following an operative procedure. The average duration of life is seven years and eight months for the eight cases.

We have divided the methods of treatment into three main groups for analysis: (1) amputation or resection with irradiation, (2) amputation or resection sine irradiation and (3) irradiation alone or with exploratory operation.

In group 1 (table 4) there are thirteen cases with a postoperative duration of life averaging 29.2 months. In three cases in this group (23 per cent) the patients were found to be well with an average duration of life of five years and seven months.

In group 2 (table 5) there are twenty-four cases with an average duration of life of twenty months. In four cases in this group (16.5

per cent) the patients are well and have an average duration of life (at the time of writing) of six years

In group 3 (table 6) there are eight cases with an average duration of life of twenty-seven months. In one case of this group (12.5 per cent), the patient is living fifty-three months after treatment. This patient's lesion was curetted prior to irradiation.<sup>33</sup>

Coley's toxins apparently have had no effect on the duration of life whether given alone or with other forms of treatment (table 7). There were three patients in the entire series who were given Coley's toxins.

TABLE 5—*Treatment by Resection or Amputation Without Irradiation*

Patient* (Surg Path Lab No.)	Color	Sex	Age	Location of Tumor	Duration of Symptoms at Time of Operation, Months	Microscopic Observations	Duration of Life Following Operation Months
35654	W	M	24	Tibia midshaft	12	Typical	11
34422	W	M	10	Tibia midshaft	4	Typical	53
34005	W	M	19	Humerus lower shaft	84	Typical	(Well after 30 months)
32174	W	M	16	Femur midshaft	6	Typical	7
29256	W	F	12	Tibia, upper shaft	12	Typical	(Well after 78 months)
28835	W	M	24	Femur lower shaft	4½	Typical	4½
28897	W	F	12	Humerus upper shaft	9	Typical	(Well after 72 months)
28395	W	M	25	Fibula lower shaft	9	Typical	1
28364	W	M	13	Fibula upper shaft	3	Typical	6½
27511	W	M	14	Femur lower shaft	6	from report	5
26915	W	M	16	Metatarsal only		Typical	36
26885	W	F	44	Tibia upper shaft	4	Typical	24
26597	W	M	39	Tarsal only	24	from report	6
24927	W	M	6	Tibia upper shaft	18	Typical	13
22795	W	M	22	Femur	24	Typical	(Well after 108 months)
15921	W	F		Pelvis only		Typical	(Died at operation)
15838	W	M	21	Humerus midshaft	5	Typical	13
15745	W	F	14	Femur, upper shaft	18	Typical	5
7963	W	M	13	Fibula midshaft	12	Typical	4½
7657	W	M	16	Fibula midshaft	6	Typical	11
5172	W	F	11	Tibia midshaft		Typical	2
4392	W	F	17	Humerus upper shaft	3	Typical	9
1207	W	F	8	Tibia upper shaft	9	Typical	9
64	W	M	21	Humerus upper shaft	6	Typical	5

\* There are four patients (16 per cent) in this group who are well averaging six years duration of life after treatment. Of this number three are living over five years.

From a study of these three tabulations there is seen to be little choice between the employment of irradiation (fig 31) or radical operation. The evidence indicates that the patient should receive a combination of both treatments when the tumor is observed in the usual location prior to metastasis.

In arriving at elements in the clinical history which would be of value in making a prognosis an analysis was made of the features presented by the living patients. Their ages ranged from 12 to 30

<sup>33</sup> Coley, W. B. and Coley, B. L. Primary Malignant Tumors of the Long Bones. Arch Surg **13** 779 (Dec) 1926 **14** 63 (Jan) 1927

years The site of involvement was either the lower or the upper extremity, including the pectoral girdle The x-ray picture showed either destruction of bone or formation of bone and sometimes both It also disclosed diffuse involvement of the bone, and either a parallel or a right angle periosteal reaction The gross pathologic changes were not unique, and both normal white cell counts and leukocytosis with

TABLE 6—*Treatment by Irradiation Alone or by Irradiation with Exploratory Operation*

Patient (Surg Path Lab No )	Color	Sex	Age	Location of Tumor	Duration of Symptoms at Time of Treatment, Months	Microscopic Observations	Duration of Life Under Treatment Months
35014*	W	F	22	Tibia, midshaft	48	Typical	(Well after 53 months)
34314	W	F	17	Femur, lower shaft	5		20
32910*	W	M	17	Tibia, midshaft	12	Typical	59
31988*	W	M	17	Femur, upper shaft	2	Typical	39
30944*	W	M	20	Tibia, lower shaft	7	Typical	5
30755*	W	M	12	Fibula, upper shaft	2	Typical	10
10537*	W	M	17	Tibia, upper shaft	6	Typical	9
5927*	W	M	7	Femur	2½	Typical	2

\* The lesions of bone in these patients, with the exception of three were explored in three the lesions were curetted and in one the tumor was treated with radium alone One patient (12 per cent of the group) is still living 53 months after treatment

TABLE 7—*Part 1 Exploratory Operation Alone*

Patient* (Surg Path Lab No )	Color	Sex	Age	Location of Tumor	Duration of Symptoms at Time of Operation, Months	Microscopic Observations	Duration of Life Following Operation, Months
34027	W	M	23	Hum alone	11	Typical	1
33807*	W	F	22	Mastoid alone	4	Typical	6
30828	W	F	9	Humerus upper shaft	13	Typical	4
30072	W	F	21	Hum alone	5	Typical	9½
29054*	W	M	7	Tibia, midshaft	7	Typical	23
28774	W	F	34	Hum	5	Typical	1 day

PART 2—*Treatment by Coley's Tumor Alone*

13439*	W	M	23	Humerus, midshaft			14
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\* The glands were excised and showed metastases microscopically typical

fever were observed Radical operation with or without irradiation and irradiation alone were among the methods of treatment

All of the patients reported in this series as living today had a preoperative duration of symptoms averaging twenty months, as against six months for those who died within a year following operation The shorter duration of symptoms apparently therefore, indicates a more rapidly growing tumor and is ground for a grave prognosis This reflects seriously on the hope of cure through early diagnosis and early treatment in a definite group of these cases Apparently, symptoms do not always precede the fatal stages of the disease by a sufficient margin for the purposes of therapeutics

Exploration does not necessarily affect the prognosis in cases in which radical operation or x-ray treatment follows exploration. In two cases (25 per cent) in which the patients are living over five years, exploration was done before the operation of choice was resorted to. In one case of curettement followed by irradiation, the patient is living over four years after treatment. In six cases in which an exploratory operation was performed without further treatment, death occurred in from one to twenty-two months. In one case in which Coley's toxins alone were given, the patient died fourteen months after the therapeutic procedure was begun.



Fig 31—*A* shows the involvement of a tibia by Ewing's sarcoma with much periosteal reaction and a mottling of the marrow cavity. This tumor was explored for biopsy, the exploratory operation being immediately followed by irradiation. *B* shows the effect of irradiation on the tumor. Marked sclerosis has occurred in both the shaft and the periosteal region, reactive bone having been formed in abundance on retardation of the growth of the tumor (no 32770, table 4).

#### NATURE OF EWING'S TUMOR

Successful analysis is dependent on a complete series of accurate observations, summarized and recorded in such fashion that connections between related facts become illumined. In order to arrive at some conception of the nature of Ewing's tumor, we have attempted such a summary in table 8.

The facts listed in table 8 point to the conclusion that Ewing's tumor is a malignant sarcoma of bone. In favor of this is the age incidence of the tumor, its location in bone, the cellular nature of the

pathologic changes, the metastases and the high percentage of fatality. Against the opinion, occasionally voiced, that this lesion is a metastatic tumor arising primarily outside of bone is the failure to demonstrate such a primary focus in any of the cases studied and the occasional cures by amputation. The cellular morphology of this tumor also does not resemble that of carcinoma, nor does the age of the patient suggest such a disease.

Opinion in favor of bone sarcoma is therefore substantiated by this study. However, the summary of the observations in table 8 is against the belief that the tumor is a myeloma originating in the marrow cavity. In the first place, as pointed out elsewhere in this paper, the

TABLE 8—*Summary of the Observations in Cases of Ewing's Sarcoma*

Observations Simulating Tumors in General	Observations Characteristic of Ewing's Sarcoma	Observations Simulating Malignancy in General
Pain and swelling	95 per cent of cases in persons under 25 years of age	Fatal in 87 per cent of cases
Limp	Duration of symptoms to time of treatment, 11½ months	
Fever leukocytosis	Trauma in from 30 to 40 per cent five months previously	Moderate anemia
Dilatation of superficial veins	Occurrence only in bone	Fever
Tender, firm mass	Tibia most frequently involved	Metastases to the lungs
Occasional regression	In long bones, shaft only primarily affected	Terminal cachexia
	Epiphysis involved only secondarily	
	Elliptical area of the shaft involvement	
	Cartilaginous bone primarily involved	
	Bulk of the tumor subperiosteal	Very cellular tissue
	Subperiosteum usually intact	
	Reactive bone both endosteal and subperiosteal	
	Cortex expanded and thickened	
	Infiltration of bone but not destruction or formation of bone primarily	
	Rapid diffusion	
	Destruction of bone late	
	Pathologic fracture rare	
	Metastases to membranous and cartilaginous bone	
	Predilection of metastases for skull	
	Tumor cells uniform in size oval or round	
	No tumor giant cells	
	No Bence Jones bodies in the urine	
	Regional glands involved	
	Conclusion	
	A neoplasm originating during the growth period in the diaphysis of bones, rapidly infiltrating bone with early diffusion involving both periosteal and endosteal reaction but producing no tumor bone or direct erosion of bone	

elliptical area of shaft involvement with the bulk of the tumor lying subperiosteally does not resemble the usual central and spherical contour of medullary tumors. Multiple myeloma, metastatic carcinoma and chloroma with leukemia all show a central location with a more or less spherical growth widening the medullary cavity. These tumors occupying the marrow cavity show early destruction of bone and with the majority of them in at least isolated instances, Bence-Jones bodies have been demonstrated.<sup>15</sup> The Ewing tumor, in contrast with these neoplasms, most frequently shows a narrowing or occlusion of the medullary cavity with both endosteal and subperiosteal formation of new bone early in the disease, which would seem to indicate that the tumor has not a primary medullary origin. The absence of marked

changes in the blood and of Bence-Jones bodies in the urine is against this assumption. Gross specimens and microscopic sections cut transversely through the bone usually show only a small portion of the tumor tissue in the marrow cavity. The rapid extension of the Ewing tumor in a plane parallel to the axis of the shaft indicates that the tumor has not the privilege of expanding freely in the two opposite directions and points to the growth's being either intracortical or subperiosteal in origin.

The majority of the observations summarized in table 8 could be explained by either an intracortical or a subperiosteal origin of the tumor. If the neoplasm is primary in the haversian systems, this would explain the rapid infiltration by the tumor producing both early endosteal and subperiosteal reactions of new bone. It would explain, also, the distribution of the tumor under the periosteum and into the medullary cavity in the later stages, and account for the widening of the haversian canals and the splitting of the layers of the cortical bone so frequently observed under the microscope (fig 32). However, conclusive microscopic proof of the origin of the Ewing tumor in the haversian canals is lacking. While specimens usually show the tumor pervading these structures we have been unable to determine whether the tumor arises here or secondarily infiltrates into these channels.

The assumption that the Ewing tumor arises in a subperiosteal locality may be maintained, with probably equal validity, from the facts observed. The active subperiosteal layer which ceases at the epiphysis and atrophies in adulthood would account for the involvement of the shaft only, in youthful patients. This locality would account also for the fact that the bulk of the tumor is under the periosteum, for the tendency of the haversian systems to be infiltrated, and for the reactive formation of new bone of both endosteal and subperiosteal origin. It would explain also the tendency of the tumor to extend up and down the shaft rather than to form a spherical growth. It would also fit in with the absence of Bence-Jones bodies in the urine and the lack of marked changes in the blood.

On the basis of these observations, it is clear that the tumor whether primarily intracortical or subperiosteal is not medullary, nor primarily osteolytic as is currently believed. The rarity of pathologic fracture, the localities affected the shaft and the gross observations are all against the assumption and destruction of bone is always a late manifestation in the disease (fig 7).

The suggestion of Kolodny following the lead of Ewing that the tumor arises about the perivascular lymphatics in the haversian canals is not altogether untenable and would give this tumor an intracortical origin. Tumor cells are frequently observed in this region (fig 33) but sections of normal bone do not show cells of the Ewing type from

which the neoplasm might arise. While we observed proliferation of cellular elements about these lymphatics in bone beneath such a condition as bursitis, the cells were of a different type and the endothelium of the lymphatics did not appear to us to resemble the Ewing cell. We



FIG. 32.—A low-power photomicrograph of a section taken through the body of the scapula. Note the splitting of the layers of cortical bone, the widening of the Haversian canals and the spicules of bone at right angles to the cortex extending inwardly from the region of the periosteum. There is a small nest of tumor cells in the medullary cavity, but the bulk of the tumor is between the cortex and the reactive bone of the periosteum near the point of medullary involvement (no. 27039, table 4).

reviewed the endotheliomas of the soft parts with all the sarcomas of the soft parts in this laboratory and did not find a tumor duplicating

in cellular character the Ewing sarcoma. The endotheliomas in the collection of Dr A R Rich in the department of general pathology, which he has gathered from the uterus, the testicle, the peritoneum, the duodenum and the liver, and the endotheliomas in our own collec-



Fig 33—A photomicrograph showing a portion of the cortex of a bone. The haversian canals have been widened by the infiltration of tumor, which has pervaded the bone by means of the perivascular lymphatics within the haversian canals (no 32174, table 5)

tion which resemble these differ markedly from Ewing's sarcoma of bone. We believe that the 'osteolytic endothelial myeloma' of Ewing is not primarily osteolytic or medullary, nor is it endothelial, although we grant the specificity of the tumor and find that the sixty cases



reported here resemble those described by Ewing, Connor and Kolodny, both clinically and microscopically

The facts at our disposal do not enable us to point out either the site of origin or the histogenesis of this tumor, and while we believe that the primary focus is specific for bone and is probably intracortical or subperiosteal, we prefer to leave the matter sub judice<sup>34</sup>

#### CASE REPORTS

**CASE 1—History**—R N, aged 19, white, a cashier was admitted to the Johns Hopkins Hospital on March 26, 1920, complaining of a lump on the left shoulder blade. She had suffered the usual ailments of childhood. The family history and the patient's previous history were otherwise noncontributory. The present illness began with a fall in February, 1918, while the patient was playing basket-ball. She struck the ground with the upper part of her back. For ten days she noticed an aching and a tired feeling in this region, but no sharp pain, swelling, tenderness or restriction of motion. In February, 1919, the patient noticed soreness in the upper part of the left arm, and at the same time the development of a lump 4 by 5 cm in diameter on the superior and medial angle of the left scapula. She did not observe any elevation of temperature or tenderness of the affected part. In May, 1919, the lump suddenly increased, and a sharp, shooting pain radiated from the region of the lump to the hand and fingers. The lump became exquisitely painful for three or four days, and then suddenly diminished in size. The pain and tenderness ceased, and the patient again felt well. Other similar attacks occurred without fever in August, September and December of 1919. On March 12, 1920, the lump suddenly increased and became exquisitely painful and tender. In this condition, the patient was admitted to the hospital.

**Physical Examination**—The patient was a healthy-looking girl of 19 years, well developed and well nourished. The mucous membranes were of good color. A review of the systems was essentially without important result save for the left scapula, where over the supraspinous part a tumor was found, 10 by 12 by 2 cm, with normal overlying skin. The tumor was a smooth, saucer-shaped mass overlying and attached to the supraspinous portion of the scapula, and extending above and medial to the superior border. The lump was not fluctuant and not tender. The blood count revealed the hemoglobin content to be 78 per cent and the white cells 7,300. The urine was essentially normal. Bence-Jones bodies were not reported. X-ray studies were made, and a diagnosis of sarcoma was considered.

**Clinical Course, Treatment**—On April 10, 1920, while the patient was in the hospital, it was deemed advisable to resect a portion of the scapula. The neck of the scapula was left intact to articulate with the head of the humerus. The patient made an uneventful recovery and returned home. On Sept 29, 1920, the patient was readmitted to the hospital, this time with a slight elevation of temperature. The patient, after going home, had steadily grown weaker. An aching pain had developed in the left shoulder following an injury to the affected part four

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<sup>34</sup> Studies are now under way to determine the exact nature of the tumor. From the radiologist's point of view Ewing's sarcoma responds like a tumor of the lymphoid group in that it reacts readily to irradiation. This is in contradistinction to the endotheliomas, which react little, if any. Histologically also the cells resemble the lymphoblast. Differential stains are being worked out to fortify further, if possible the position that Ewing's sarcoma may be of lymphoid nature.

weeks prior to admission. The tumor had reappeared and was rapidly growing. Treatment with radium was deemed advisable.

On May 21, 1921, the patient died. Before death, she had dwindled to a mere skeleton, was practically paralyzed and was having severe attacks of pain about every seven hours.

*Gross Pathologic Changes*—The specimen consisted of the medial five sixths of the scapula. A tumorous mass involving the middle half of the superior margin, together with the supraspinous fossa and subscapular fossa was noted. It was fairly circumscribed, although not encapsulated. Along the advanced margin, the tumor appeared between the periosteum and the bone. On section, the surface was a clear gray with a few yellow opaque areas. The medullary cavity appeared to be less involved. No hemorrhagic areas were seen, and grossly there was little stroma, nor were trabeculae involving the tumor areas observed.

*Microscopic Observations*—Much fibrous stroma, with areas of small, round and ovoid cells, the nuclei of which varied slightly in size was noted, with little or no intercellular stroma. The cellular structure was typical of Ewing's tumor. Bone spicules were noted, most of which were being destroyed by tumor cells. An area of periosteum was seen with a layer of new bone formed beneath it, which in places was separated distally from another layer of bone by tumor cells.

*CASE 2—History*—L. J. W., aged 34, white, a housewife, was admitted to Johns Hopkins Hospital on July 14, 1921, complaining of trouble with the back and the hip. The family history was noncontributory, the patient's previous history revealed an attack of phlebitis in the left leg following the birth of a child, about a year before admission. In 1909 and again in 1915, tonsillectomy was performed, and the patient had had the right antrum drained in 1915.

The illness in question began in September, 1920, with a pain in the region of the coccyx, especially on walking. She limped with the right leg and for two months previous to admission had suffered sharp pains in this limb on movement, accompanied by a sensation of "giving way" in the lumbar region.

*Physical Examination*—There was pain on pressure over the right sacro-iliac joint. The fifth lumbar vertebra was more prominent than usual. All deep reflexes were slightly hyperactive. X-ray examination revealed a large area of destruction in the ilium involving the sacro-iliac joint. The sacrum was not involved, and apparently there was no bony reaction surrounding the area of destruction. The blood count showed white cells 6,500 and red cells 4,160,000, with a hemoglobin content of 90 per cent. Polymorphonuclear cells were 64 per cent. The urine was normal. Bence-Jones bodies were not reported.

*Treatment and Clinical Course*—The patient was put in a brace and discharged to return in six weeks. On Aug. 30, 1921, she returned to the hospital because of a wrench of the back, she was suffering intense pain. The physical examination revealed nothing more than had been noted before. The laboratory observations were again within normal limits. On Sept. 7, 1921, a swelling the size of a walnut was noted attached to the skull just to the right of the midline on the anterior portion of the head. The nodule was slightly sensitive. X-ray pictures showed two small areas of destruction in the parietal bone. On Sept. 8, 1921, an exploratory operation was done. The right ilium was exposed, the fascia covering the sacro-iliac joint was opened and a considerable amount of clotted blood escaped. At one point the bony pelvis was apparently eroded through. The patient left the operating room in a state of shock and died on Sept. 9, 1921. At no time was there an elevation of the temperature.

*Microscopic Observations*—A homogeneous mass of small round cells with slightly vesicular nuclei was noted. The chromatin content of the nuclei was moderate with no particular arrangement. There was little connective tissue framework, and the tissue was not vascular, only a few blood vessels being noted.

*CASE 3—History*—W H R, aged 17, white, a machinist, was admitted to the Johns Hopkins Hospital on April 27, 1910, with a complaint of swelling and lameness in the right leg. The family history and the patient's previous history were noncontributory. The illness had begun six months previous to admission, when the patient noted intermittent pain in the right leg. The pain persisted for about two days and then disappeared for about two weeks. The intervals between the attacks of pain became shorter until four months before admission, then the patient began to have pain in the right leg every night. The pain was piercing, and prohibited sleep. Five months before admission, swelling was noted at the site of the pain, and two months before admission, the swelling was curetted at a neighboring hospital. The wound, which exuded serosanguineous fluid for a time, finally healed. Shortly after the operation, the pain recurred, the patient having many wakeful nights. The patient ceased to walk because of a painful right knee. Subsequent to the onset of his illness, he noticed a loss of weight amounting to 15 pounds (6.8 Kg).

*Physical Examination*—The physical examination revealed a poorly nourished boy. The right inguinal glands were enlarged and hard, but there was no enlargement of the glands in general. The right leg, thigh and knee were distinctly larger than the left. A fusiform swelling below the knee was noted. A scar 10 cm long was seen over the upper part of the right tibia. On palpation, the tibia appeared thickened, but fairly smooth, nowhere was it fluctuant. Over its upper portion, tenderness was easily elicited. Voluntary motion of the leg was good. Laboratory examination revealed white blood cells, 12,000, red blood cells, 6,000,000, hemoglobin 65 per cent, polymorphonuclears, 75 per cent. The urine was normal. No Bence-Jones bodies were reported.

*Treatment and Clinical Course*—Coley's toxin was given from time to time as a postoperative measure, and x-ray treatment was administered twice weekly for a time. The temperature was elevated on admission, and at no time later was it noted as normal, it reached 103 F, excluding the reactions caused by Coley's toxin. The patient died on Nov 2, 1910, with metastases to the skull and to the glands of the groin.

*X-Ray Observations*—The x-ray picture showed a definite periosteal formation of new bone resembling somewhat that seen in syphilitic periostitis or in the involucrum about a chronic osteomyelitis. Between the bone shadow and the periosteal growth there were more light shadows than one expects in x-ray pictures of syphilis or of osteomyelitis. The shadow of the medullary cavity of the upper third of the tibia was irregular.

*Microscopic Observations*—Areas of small round cells were surrounded by fibrous stroma. There were also areas of old bone and hemorrhage. There were numerous cavities chiefly in the cellular areas. In places, the fibrous stroma was cellular, while in other areas the fibrous stroma had a marked amount of eosin-staining intercellular substance.

*CASE 4—History*—J B, aged 10, white, a school girl, was admitted to the Johns Hopkins Hospital on Dec 6, 1919, complaining of intermittent pain in the leg. The family history and the patient's previous history were noncontributory. The present illness began about one year before admission to the hospital with cramps in the lower part of the left leg, not severe, and lasting for only a short

time, with recurrences several months apart. Two weeks before the patient's admission, the mother noticed that the child's left leg was a little larger than the right leg, and she immediately sought medical consultation.

*Physical Examination*—The results of physical examination were negative at this time save for the condition of the affected part. The left calf was distinctly enlarged, especially at the outer side. On palpation, a mass was felt along the fibula extending from 6 cm below the knee to 6 cm above the external malleolus. It was fusiform, reaching its maximal size at the region of the calf. The tumor mass was bony, not tender but immobile, and the surface was apparently rough. The inguinal glands were hard and shotty on both sides, but more so on the right. There was no elevation of temperature locally over the tumor mass. The blood count showed white blood cells, 9,860, red blood cells, 4,864,000, hemoglobin, 75 per cent, polymorphonuclears, 62 per cent. The Wassermann reaction was negative. The urine was normal. Bence-Jones bodies were not sought for.

*Treatment and Clinical Course*—On Dec 11, 1920, the fibula was excised together with the area of tumor. The leg was then irradiated. The patient made an uneventful postoperative recovery and returned home. On Aug 1, 1928, the patient was readmitted to the hospital for large and painful glands of the left groin, the glands being the size of hickory nuts. At this time, the edge of the liver was felt 3 fingerbreadths below the costal margin, although the lungs were apparently normal. The lymph glands were removed and on section were found to contain tumor. The leg was irradiated at Dr Howard A. Kelley's Hospital, but the clinical course was continually downhill and the patient eventually succumbed with diffuse internal metastases. After the patient's admission to the hospital, the temperature ranged from 99.4 to 100 F.

*Gross Pathologic Observations*—The specimen consisted of the lower two thirds of the fibula, which contained a tumor mass. The periosteum was thickened above and below the mass and appeared to be continuous with the capsule surrounding the tumor. The bone was eroded as though worm eaten, and the bony trabeculae were seen running at right angles to the shaft into the subperiosteal tumor mass. The tumor was well circumscribed by the attenuated periosteum.

*Microscopic Observations*—The tumor was composed of much fibrous tissue surrounding areas of round and ovoid cells of uniform size. The cytoplasm of the cells was indistinct, staining a pale pink with eosin. An occasional area of old bone was seen surrounded by tumor cells. Giant cells were not seen.

*CASE 5—History*—W. S., aged 21, white, was admitted to the Johns Hopkins Hospital on Oct 21, 1913, complaining of a swollen left shoulder. The family history and the patient's previous history were nonessential. The present illness had begun five months prior to admission with a small lump in the left shoulder which gradually grew until it had reached considerable size. For the last three months before admission the shoulder had been painful both day and night, but the nocturnal pain was the more severe. There was no history of trauma.

*Physical Examination*—Examination revealed nothing of interest save at the site of the lesion. Over the head of the left humerus was a large, almost spherical swelling roughly as large as an orange. It was everywhere smooth and indurated but not bony. On palpation it appeared to be directly continuous with the shaft of the humerus. There was definite atrophy below the elbow joint. There was no general or local elevation of the temperature.

The blood count showed white blood cells 11,600, hemoglobin 87 per cent, polymorphonuclears, 52.8 per cent. The urine was normal. Bence-Jones bodies were not sought.

*Treatment and Course*—On Oct 28, 1913, resection of the upper end of the humerus was done with a subsequent transplantation of bone. Early in 1914, amputation was performed. The patient died from the tumor in September, 1914.

*Microscopic Observations*—Although sections are not available at the time of writing, Bloodgood, in a recent classification, placed this tumor microscopically in the Ewing sarcoma group.

*CASE 6—History*—J F B, white, aged 22, was admitted to the Johns Hopkins Hospital on Jan 8, 1918, complaining of pain and swelling in the region of the left knee. The family history and the patient's previous history were non-contributory. The present illness had begun two years before admission with pain, which was more or less persistent. One month later, a swelling was noted in the region of the right knee. Six months prior to entry, the patient joined the army, his condition having been overlooked. Six weeks prior to hospitalization, the patient consulted an army surgeon because of pain in the knee on riding a horse.

*Physical Examination*—Examination revealed nothing of importance save a swelling above the knee surrounding the lower end of the femur. On palpation, an irregular, hard mass was felt, but there was no tenderness or edema of the soft parts. The glands in the left groin were larger than normal. The popliteal artery was easily palpated over the tumor mass. There was some limitation on flexion of the joint.

*Treatment and Clinical Course*—Soon after admission of the patient to the hospital, the involved leg was amputated just below the trochanter of the femur, the glands in the groin were removed. The patient at the time of writing has remained well, without irradiation, for nine years following the operation.

*Gross Pathologic Observations*—The specimen consisted of the greater part of the femur, which had been sectioned longitudinally. The lower part of the femur was encircled by a periosteal growth, largest on the posterior side of the femur, with considerable thickening of the cortical bone. There were spicules of bone radiating out into the tumor at right angles to the cortical bone (fig 7). The deeper or intercortical surface, the cancellous bone and marrow cavity appeared grossly normal.

*Microscopic Observations*—The tumor was composed of small round cells arranged in large alveoli, separated by dense fibrous tissue. In the tumor cells, many cross and longitudinal sections of thin walled blood vessels containing blood were noted. Bone lamellae were observed within the fibrous tissue between the areas of tumor cells.

*CASE 7—History*—M R, white, aged 8, a school girl, was admitted to the Johns Hopkins Hospital on Jan 17, 1896, complaining of an injury with subsequent tenderness and swelling of the upper part of the left leg. The family history and the patient's previous history were noncontributory. The present illness had begun nine months before admission, when the patient fell on the left leg. It became tender for a few days and then apparently was well. Three months before the patient's admission, the mother noticed a swelling in the anterior portion of the lower part of the child's leg, and the child complained of some pain that was much worse at night. The tumor gradually increased in size, occasionally regressing, only to become again somewhat larger.

*Physical Examination*—The patient was a well nourished girl, presenting nothing abnormal save at the site of the lesion. Over the upper third of the left tibia, a swelling was noted apparently not involving the head of the bone. The swelling was firm and tender, the skin was normal, except for the increase in the size of peripheral vessels and slight edema in the region of the tumor mass. The

temperature of the patient while she was in the hospital, ranged between 98.6 and 100 F. The blood count was within normal limits. The urine showed no abnormality.

*Treatment and Clinical Course*—Amputation was performed soon after the patient's admission. Eighteen months after the injury, nine months after the operation, the patient showed metastases to the cervical vertebrae and subsequently succumbed to the tumor.

*Gross Pathologic Observations*—A periosteal growth began at the middle of the tibia and extended to the epiphyseal line. The periosteum was thickened but not perforated. The tumor showed a fine, grayish-white, granular growth containing spicules of bone. The shaft of the bone was invaded by the growth. There was little formation of new bone and considerable destruction of bone.

*Microscopic Observations*—The tumor was composed of small round cells, some of which were arranged in small alveoli. The compartments of cells were separated by strands of fibrous connective tissue.

**CASE 8—History**—I. C., white, aged 6, was admitted to the Johns Hopkins Hospital on Aug. 20, 1919, complaining of pain in the left leg. The family history was noncontributory. The patient had suffered an injury to one leg (side not mentioned) at the age of  $1\frac{1}{2}$  years, otherwise the history was without bearing. The illness in question began one year before admission, with pain in the left leg and a slight fever. There was no redness or swelling over the surface of the leg. The fever subsided in a few days, and there was no further trouble until Aug. 13, 1919. Then the lower part of the left leg became red, swollen, painful and hot.

*Physical Examination*—Examination revealed a white boy, with a slight general glandular enlargement. Results of the general physical examination were otherwise negative except for the condition at the site of the lesion. The left leg was swollen from the knee to a point just above the ankle. The overlying skin was tense but not reddened. There was no increase in surface temperature. On palpation, a firm, indurated mass, not tender and not fluctuant, was noted in the region of the left tibia, apparently continuous with the sheath of the tibia. An x-ray picture showed a lesion similar to syphilitic osteomyelitis. The temperature during the period of admission ranged between 99.4 and 101 F. Laboratory observations were not reported in this case except for the urine, which was normal. Bence-Jones bodies were apparently not sought. The white cell count was 13,000.

*Treatment and Clinical Course*—The patient died of tumor in September of 1920, one year and one month after the operation.

*Microscopic Observations*—The tumor was composed of small, round and oval cells staining a uniform deep blue. No nucleoli were seen in the nuclei, and little or no cytoplasm was found. There were numerous small blood vessels traversing the section of the tumor.

**CASE 9—History**—W. L. G., white, aged 20, a laborer, was admitted to the Johns Hopkins Hospital on April 6, 1907, complaining of pain about the coccyx. The family history and the patient's previous history were noncontributory. The present illness had begun seven months before admission with trauma to the right hip, a slight pain having been felt in the coccygeal region for a short time previously. The pain became more frequent after the trauma. Four months before admission, it became constant and concomitantly the patient noted a beginning lameness with the formation of a tumor in the region of the hip. He also noticed a loss of 20 pounds (9 Kg.) in weight over a comparatively short period of time. Defecation and urination became painful.

*Physical Examination*—The patient was a young white man with considerable loss of subcutaneous fat. The glands in the neck and in the groin were enlarged. The results of the general physical examination were otherwise negative, except for the condition at the site of the lesion. On the dorsum of the right ilium, a smooth, hard, round swelling extended to the right margin of the sacrum. The blood and the urine showed nothing of unusual interest. There was no record of Bence-Jones bodies. Previous to admission an exploratory operation had been performed at a neighboring hospital. On admission to the Johns Hopkins Hospital, the condition was found to be inoperable, and only enough tissue was removed for diagnosis. This patient was not heard from subsequently.

*Microscopic Observations*—The tumor was composed chiefly of small, round cells of the Ewing type. In places, these cells were separated by bands of eosin staining fibrous tissue. Here and there we saw hemorrhage and coagulation necrosis. Giant cells were not seen.

CASE 10—*History*—S. H., a white man, aged 24, was admitted to the Johns Hopkins Hospital on Nov. 3, 1892, complaining of pain in the upper part of the left arm. The family history and the patient's previous history were noncontributory. The illness had begun in May, 1892, six months prior to admission, with pain in the left deltoid region, which at times was severe, with aching and throbbing. Two and one half months before admission, following a strain of the left arm, swelling began and gradually increased with, at the same time, extreme tenderness on pressure. There was edema of the lower part of the arm and of the hand, which remained constant after the swelling in the arm had become noticeable.

*Physical Examination*—The results of the examination were negative save for the affected limb, which showed a swelling in the middle third of the humerus extending to and above the shoulder joint and into the axilla. The skin over this tumor mass was edematous and red. The blood and the urine at this time were normal. Bence-Jones bodies were not reported.

*Treatment and Clinical Course*—On Nov. 3, 1892, an exploratory operation was performed, and a diagnosis of sarcoma was made. Amputation at the shoulder joint followed a few days later. Metastases to the glands were found in the axilla at this time. Death occurred a few months later from internal metastases.

*Microscopic Observations*—The tumor was composed of small, round cells, well preserved about the blood vessels, in places, with peripheral necrosis, while in many areas one found masses of tumor cells with no particular arrangement. Strands of fibrous tissue were seen dividing the tumor into compartments. Spicules of bone were undergoing absorption surrounded by the tumor cells.

CASE 11—*History*—M. C., white, aged 17, a housewife, was admitted to the Johns Hopkins Hospital on Aug. 20, 1902, with a complaint of pain in the upper part of the right arm. The family history and the patient's previous history were noncontributory. The illness had begun three months before hospitalization with pain between the elbow and the shoulder of the left arm. There was no history of trauma. A concomitant swelling the size of a hen's egg appeared in the same region. The swelling was first poulticed, later aspirated and then, six weeks later, incised, a blood clot being removed. The tumor grew rapidly following the incision. One week before admission, the skin over the tumor became bluish and edematous. Another incision was made, and this had not healed at the time of admission. The pain was intermittent and of varying severity, it usually was a dull shooting pain. There was considerable edema of the right forearm at times.

*Physical Examination*—The patient was well nourished, and apparently in the best of health, except for pale mucous membranes. The affected limb revealed a fusiform tumor a little below the middle of the upper part of the right arm, over which, in part of its extent, a scar and an ulcerated area were found. The tumor mass was apparently firmly attached to the humerus, it was not tender and not painful. The temperature following admission ranged from 99 to 100 F. The urine revealed nothing of interest. Bence-Jones bodies were not reported. The hemoglobin content of the blood was 75 per cent.

*Treatment and Clinical Course*—On Aug. 22, 1902, the arm was amputated at the shoulder joint. The patient made an uneventful recovery. A few weeks later, some enlarged axillary glands were removed, which showed metastases. The patient apparently did well for a time. Then there was a gradual recurrence in the stump. The patient became emaciated, the area of the right breast became involved, and the patient died of tumor nine months after the operation.

*Gross Pathologic Observations*—A spindle-shape tumor surrounded the shaft of the humerus. The shaft was roughened. In the tumor tissue between the shaft and the periosteum, there were islands of bone of irregular shape, and the cylinder-like blood vessels were filled with blood clot. The greater part of the tumor was so hemorrhagic that its character could not be made out. The nonhemorrhagic portion was pearly white, finely granular and friable. The entire tumor was encapsulated from the surrounding muscles.

*Microscopic Observations*—The tumor was composed chiefly of small, round or elongated cells, with no giant cells. In places, a perithelial arrangement could be made out. There was a great deal of hemorrhage between the cells, and there were large vessels filled with blood.

CASE 12—J. H. C., white, aged 24, a farmer, was admitted to the Johns Hopkins Hospital on March 19, 1899, complaining of pain and discomfort in the right leg. The family history was of interest only in that it revealed considerable tuberculosis in the family. The patient's history previous to the illness was negative. The illness in question had begun three years before with trauma of the right leg. The same leg was retraumatized one year later, when the patient fell and fractured the right femur. There was no swelling or other evidence of tumor, and the leg was treated for simple fracture. But apparently the leg did not heal. Nine months before admission, an operation was performed and much macerated tissue and about a quart of stained fluid was removed from the affected limb. Subsequently an amputation was performed. The patient had become emaciated and weak, but after the operation he gained in weight and was about on crutches until one week before the admission under consideration. Then the stump was aspirated and an amount of bloody fluid was removed.

*Physical Examination*—The patient was poorly nourished and emaciated, but otherwise apparently normal, except for the right stump. This was enlarged and swollen, with many dilated veins at its distal portion. The line of incision was normal. The tumor mass in the region of the stump was hard, resilient and uniform throughout. The surface was smooth. There was good motion in the hip joint.

*Treatment and Clinical Course*—On March 24, 1900, the leg was amputated at the hip joint, and the iliac glands were excised. One month later, there was a local recurrence, with clinical manifestations of internal metastases. The patient succumbed to the metastases. The temperature during the period of admission had ranged within normal limits.

*Gross Pathologic Observations*—An encapsulated tumor almost completely filled the amputated stump. Nothing was left of the bone but the articular car-



tilage of the head of the femur. The tumor was composed of a meshwork of fibrous tissue, in the cavities of which was seen friable, hemorrhagic, granular tissue. Much destruction of bone was noted, but no formation of new bone.

*Microscopic Observations*—The infiltrating border of the tumor was composed chiefly of small, round and elongated cells with typical nuclei (containing a sparse scattering of chromatin granules). The tumor cells were arranged around cavities filled with blood, in some spots, the perivascular arrangement was beautifully preserved. No pleomorphism was observed, and no intercellular stroma was noted. Septums divided the tumor into lobules, a phenomenon often seen in soft parts invaded by the tumor.

**CASE 13—History**—P. S., white, aged 11 years, a schoolgirl, was admitted to the Johns Hopkins Hospital on Nov. 23, 1903, complaining of a tumor of the left leg. The family history and the patient's history previous to the illness were noncontributory. The illness had begun six months prior to admission, when the patient received a trauma of the lower part of the left leg and another slight trauma soon afterward. At that time, soreness developed in the bruised portion of the leg, which became swollen and looked much inflamed. There was a slight elevation of temperature. The swelling was progressive, the skin became red and streaked in places. Two months before admission, the leg became painful, the nocturnal pain being more severe than the diurnal pain. On Oct. 1, 1903, a physician was consulted, who advised blistering of the leg. At a later date, he incised the tumor area. Soon after this the pain recurred with increasing severity. Another physician was consulted, who operated immediately, incising the bone. Pain decreased for a few weeks and then returned in a more severe form and remained constant until the admission under consideration.

*Physical Examination*—The patient was pale and thin, and had lost much subcutaneous fat. She had a slight enlargement of the glands of the groin. The results of a general physical examination were otherwise negative save for the lesion on the left leg, which showed a spindle-shaped enlargement in the region of the tibia. On its anterior surface, a large mass protruded, appearing ulcerated with much erosion of tissue. The area was covered by a foul-smelling, yellowish discharge.

The blood at this time revealed a leukocyte count of 15,000 with hemoglobin 40 per cent. The urine was normal. Bence-Jones bodies were not recorded. The temperature subsequent to admission ranged from 99 to 100 F.

*Treatment and Clinical Course*—On Nov. 24, 1903, the leg was amputated through the thigh region. The patient made an uneventful recovery. However, a few weeks after the amputation, metastatic nodules were noted in the right occipital and temporal regions of the skull, with some spasticity of the extremities. The patient succumbed eight weeks after the operation. An autopsy was not permitted.

*Gross Pathologic Observations*—A tumor entirely surrounded the left tibia. The upper portion of the tibia was considerably expanded. The greater part of the tumor was necrotic and dirty, yellowish green, with a foul odor and a cheesy consistency. Those portions of the tumor that were well preserved were soft, and a thick cellular fluid could be scraped from their surfaces. The compact bone was much thinned, and the medullary cavity was filled with material looking like the rest of the tumor.

*Microscopic Observations*—A mass of small, round and ovoid cells with indistinct cytoplasm was observed. The nuclei were sparsely granular without any particular chromatin arrangement. There were areas of hemorrhage with an occasional well preserved blood vessel. Formation of new bone was not noted but old bone was being resorbed.

# PANCREATIC BLADDER IN THE DOMESTIC CAT

REPORT OF A CASE \*

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AND

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While conducting a series of observations on the effect of intravenously injected emulsified fat on the emptying of the gallbladder of cats, we fortuitously encountered a case of pancreatic bladder. Although twenty-three cases of well defined pancreatic bladders have been recorded in the literature during the last twenty-three years, the anomaly is exceedingly rare, it appears only in the domestic cat. Since this is the first time an anomaly of this sort has been observed in our laboratory, and since its structure so satisfactorily supports the hypothesis of a pancreatic origin, we are including the description of the case in the slowly accumulating literature on aberrant pancreatic lobes and vesicles.

Boyden<sup>1</sup> (1925) not only described six new cases of the aberrant variation, but presented for the first time adequate histologic and embryologic data in support of the origin for pancreatic bladders wholly independent of the extrahepatic biliary system. Bean and Dreyer<sup>2</sup> (1927) have added additional histologic data to our knowledge of pancreatic bladders. These authors made a unique contribution in that they showed in their second paper a case of double pancreatic bladder in which a smaller vesicle was embedded in the wall of the primary one. Although they recognized a difference between the gallbladder and the primary pancreatic bladder, yet in their opinion the identity of the smaller pancreatic bladder and gallbladder was sufficient to establish an hepatic origin for both vesicles. Boyden<sup>3</sup> (1929) however showed the error of this conclusion by calling attention to their published illustration in which clusters of glands lie within the tunica muscularis of

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\* From the Division of Experimental Surgery and Pathology. The Mayo Foundation

1 Boyden E A. The Problem of the Pancreatic Bladder: a Critical Survey of Six New Cases Based on New Histological and Embryological Observations, *Am J Anat* **36** 151 1925

2 Bean, R J, and Dreyer N B. A Pancreatic Bladder in the Cat. Structurally Analogous to the Gallbladder. *Tr Nova Scotia Inst Sc* **17** 63 1927, Duplication of Pancreatic Bladder and Accessory Pancreas in the Cat. *Anat Rec* **36** 155 1927

3 Boyden Edward A. A Note on the Origin of Pancreatic Bladder. *J Anat* **63** 353 1929

the secondary vesicle. Such structures do not exist in the gallbladders of cats, but are common to pancreatic vesicles, thus Boyden concluded that the explanation that these vesicles are of pancreatic origin is still satisfactory. Hitherto, some students of the problem of pancreatic bladders had ascribed to them an origin essentially hepatic, since they were thought to arise through clefts in the gallbladder or extrahepatic tract. Earlier consideration of the anomaly had not included any essential differentiation in the morphology of the hepatic and pancreatic vessels, and they had been regarded as derivatives of one and the same structure, although Miller<sup>4</sup> (1910) had claimed that possibly their origin was from the ventral pancreas. Lewis<sup>5</sup> (1911) ventured the suggestion that pancreatic bladders are really double gallbladders, arising from a subdivided hepatic diverticulum, which empties into subdivided cystic and common bile ducts. In the development of the extrahepatic biliary tract in man, the facts may warrant the assumption that such duplication as does occasionally exist may have its explanation in the double lumen which arises following the solid stage of the bile duct. Double gallbladders and split cystic and common ducts in man, occasionally reported in the medical literature, no doubt have an adequate embryologic explanation. On the other hand, it is extremely difficult to account for these aberrant pancreatic structures in the porta hepatis of the cat on the basis of the embryogenesis of the hepatic diverticulum.

Boyden<sup>6</sup> (1926), in a careful study of the development of the hepatic structures in the cat, could not recognize at any time a solid stage of either the common or the cystic ducts. This is interesting in the light of the fact that cases involving split cystic or common ducts have never been observed in this animal, and is rather conclusive evidence that whatever such splitting does exist in other animals a cleft arising in the solid ductus cysticus or choledochus has occasioned the splitting. The gallbladder in cats, on careful study of the development of the hepatic structures in the cat, could not recognize at any time a solid stage of either the common or the cystic ducts. This is interesting in the light of the fact that cases involving split cystic or common ducts have never been observed in this animal, and is rather conclusive evidence that whenever such splitting does exist in other animals a cleft arising in the solid ductus cysticus or choledochus has occasioned the splitting. The gallbladder in cats, on the other hand, possesses these solid stages during

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4 Miller, W. S. Pancreatic Bladders, *Anat. Rec.* **4** 15, 1910.

5 Lewis, F. T. The Bi-Lobed Form of the Ventral Pancreas in Mammals, *Am. J. Anat.* **12** 389, 1911.

6 Boyden, E. A. The Accessory Gallbladder. An Embryological and Comparative Study of Aberrant Biliary Vesicles Occurring in Man and the Domestic Mammals, *Am. J. Anat.* **38** 177, 1926.

its embryonic growth for in the 15 mm embryo the entire lumen involving both the fundus and the neck, is filled with a solid core of cells proliferated from the simple columnar epithelium. Subsequently isolated clefts arise in this core, at first discontinuous they ultimately fuse increase in size and restrict the original core of cells to slender trabeculae until at the 38 mm stage the distended form of the vesicle has been restored and it is hollow throughout. It would appear that the existence of paired ducts and vesicles, as in these pancreatic anomalies must have an explanation other than that first suggested by Lewis. Were it not for the finer histologic disparity that really does exist between the biliary and the pancreatic bladder the case of Beckwith<sup>7</sup> (1920), in which the vesicles of the cat are confluent at the necks, might have its explanation in a subdivided hepatic organization. And yet the paired ducts, continuing from their point of confluence independently backward the one to the choledochus and the other to the ventral lobe of the pancreas, do not have a common origin in the light of newer knowledge of the embryology of this region in the cat. Accordingly, one may only postulate that in the Beckwith case a fistulous communication had been established between the two structures hitherto independent.

In the case of pancreatic bladder under consideration, the two vesicles, as well as their ducts, were entirely independent down to the region of the ampulla, and in this sense is more or less identical to the instance recorded by Mayer<sup>8</sup> in 1815. Pursuant to another study the cat was killed by a severe blow on the head, and opened and explored immediately. Lying closely adjacent to the gallbladder, and suspended from it by a double fold of mesentery, was this flask-shaped pancreatic vesicle (fig 1). It was pure white and presented a striking contrast to the dark bluish-green gallbladder lying just dorsal to it. The vesicle was relatively well distended with a whitish fluid of watery consistence, which could be expressed into the duct readily since the vesicular wall was far less resistant to pressure than the tunic of the gallbladder. With the hypodermic needle the white fluid was withdrawn carefully tested and found to be pancreatic juice as judged by its proteolytic action. There was no evidence of bile in the fluid content of the vesicle.

Organic continuity did not exist between the two vesicles at any point. They were more closely adherent, however at the level of the neck of the gallbladder where the two vesicles were firmly bound by bands of fibrous tissue, one is forced again to recall the Beckwith case in which a confluence had been established between the two structures at this level.

7 Beckwith, Cora I. Note on a Peculiar Pancreatic Bladder in the Cat. Anat. Rec. 18: 363, 1920.

8 Mayer, A. C. Blase für den Saft des Pankreas. Arch. f. d. ges. Physiol. 1: 297, 1815.

In this case, however, the tunic of one could be readily freed from the tunic of the other, thus the two structures should be recognized as organically distinct, arising from divergent anlagen. It is not altogether improbable that had this animal continued to live for a considerable period a fistulous communication might have arisen between the two structures at this point, thus producing a condition identical to that described by Beckwith.

Below the approximated necks of the two vesicles, the respective ducts diverge somewhat and pursue their independent course to the

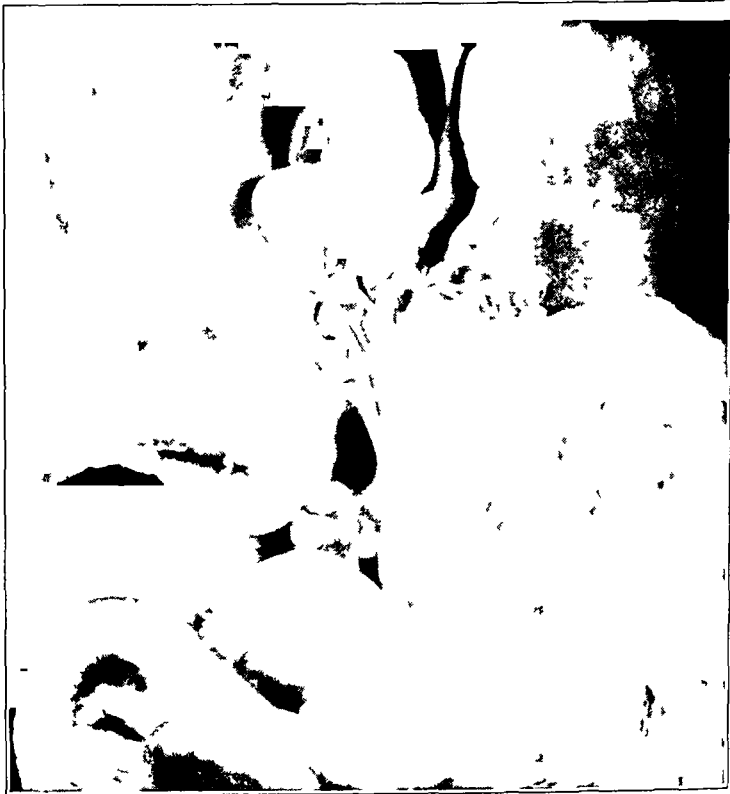


Fig 1—Liver and duodenum of the cat. The pancreatic bladder (left) is suspended from the larger gallbladder.

duodenum (fig 1). The choledochus, receiving the hepatic ducts, enters the wall of the duodenum at the customary level and opens by way of the ampulla into the gastro-intestinal tract. The pancreatic duct, on the other hand, enters the anterior extension of the ventral lobe of the pancreas, joins the duct of Wirsung and subsequently unites with the choledochus at the ampulla. In this cat, the ventral lobe of the pancreas extended forward to the level of the pylorus, at which point the duct coming from the vesicle entered pancreatic tissue.

The microscopic evidence in this case of pancreatic bladder entirely substantiates the conclusions of Boyden, and since there is such disparity

between the finer organization of the two vesicles it seems advisable to present this additional data which can hardly be explained on the hypothesis of a "split" gallbladder.

Both pancreatic and biliary vesicles were fixed with formaldehyde and maintained in the approximate state of distention in which they were encountered. Accordingly, the relative thickness of the respective tunics has not been essentially altered by fixation or procedures of technique. Sections were stained with hematoxylin and eosin, and with van Gieson's stain.

Sections taken through the approximate center of the gallbladder passing through the fundus of the pancreatic vesicle revealed at once the dissimilarity in the finer organization of the two structures (figs 2 and 3). True both of them possess the tissues characteristic of biliary

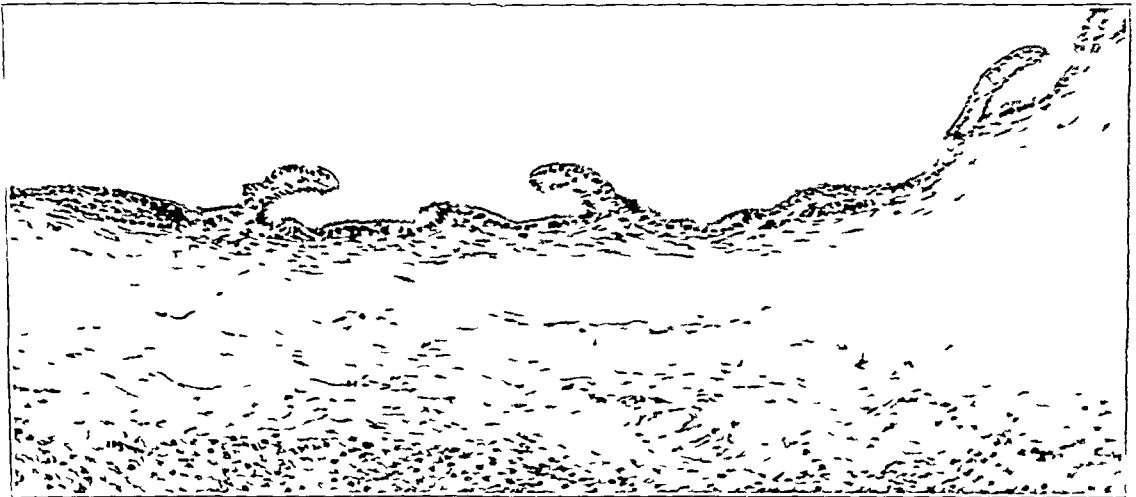


Fig 2—Section of the wall of the gallbladder through the approximate center of the vesicle,  $\times 150$

vesicles and both possess rugae of varying proportions extending into the lumen but in the finer details the two are essentially different. The wall of the pancreatic vesicle is from three to five times as thick as that of the biliary vesicle—a discrepancy due more essentially to the larger extent of the tunica propria in the former. The folds of the mucosa extending into the lumen of the pancreatic vesicle are triple the proportions of those of the gallbladder. In the latter the rugae are of about uniform height, seldom branch and rarely if ever unite at their tips. Even in the greatly contracted gallbladder (Boyden<sup>9</sup> 1925) the folds

<sup>9</sup> Boyden E. A. The Effect of Natural Foods on the Distention of the Gallbladder with a Note on the Change in Pattern of the Mucosa as It Passes from Distention to Collapse. *Anat Rec* 30: 333, 1925.

appear more filiform in section and have only a slight tendency to branch. In contrast, the rugae of the pancreatic bladder are of varying heights and frequently they branch, or become contiguous at their tips, forming thereby enlarged crypts below the mucosa. Furthermore, the cells forming the axes of these folds of the pancreatic mucosa are more loosely arranged than those in the gallbladder, where the tunica propria forms a solid more or less compact structure. Scattered cells, perhaps of the histiocyte series, abound throughout the extent of the submucous coat in the pancreatic vesicle. These could not be recognized in the tunica of the gallbladder.

Cells comprising the mucosa of the pancreatic vesicle are of the high columnar type with large spherical nuclei basally placed. The cyto-

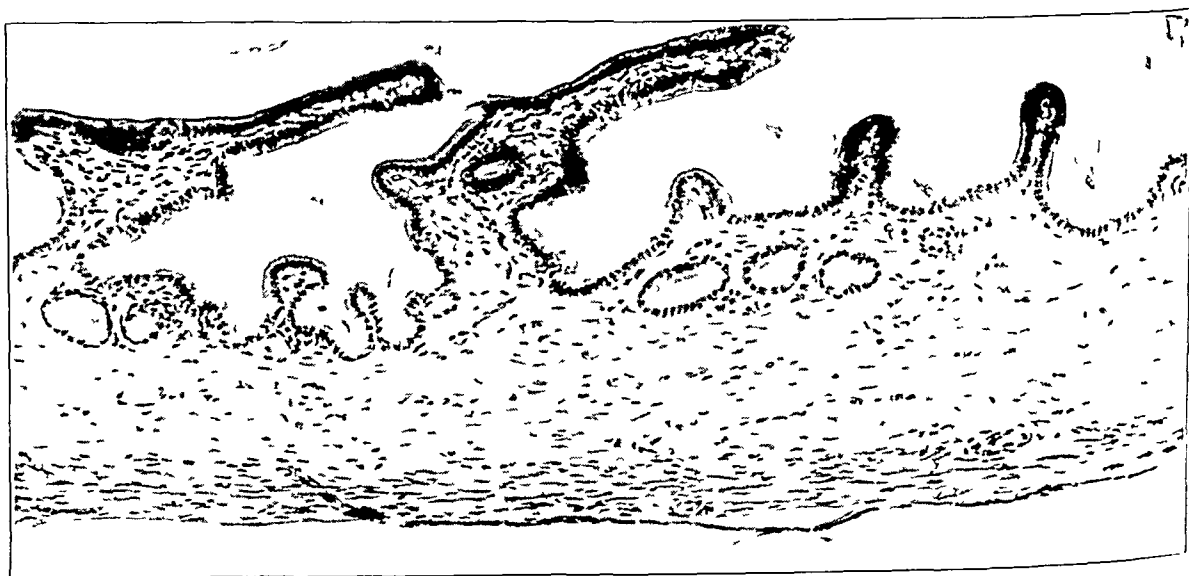


Fig 3—Section of the wall of the pancreatic bladder through the region of the fundus,  $\times 150$

plasmic bodies are extensively vacuolated, spongy or alveolar in content and in marked contrast to the granular cytoplasm of the mucosa of the gallbladder. Whether these cells constitute an absorbing or a concentrating mechanism, similar to that in the gallbladder, can only be postulated. The extensive vascularity of the vesicle, however, may suggest that the fluid contents, or portions of it, found its way into the organ by an absorptive route.

As indicated, all layers of the pancreatic vesicle are considerably thicker than corresponding portions of the wall of the gallbladder. Muscle fibers, however, are relatively scarce, and they are intertwined with the elastic fibers of the serosa and cells comprising the tunica propria so that it is difficult to differentiate muscularis as such.

Adjacent to the muscle cell area is the serosa, consisting of a dense fibrous coat through which the larger vascular channels and the outer peritoneal layer course

The neck of the two vesicles are equally distinctive in their organization, and apparently the structures are wholly independent in origin. The neck of the pancreatic bladder is simple in structure, and is only a reduction in size of the distended fundus, whereas the neck of the gallbladder resembles in every way that of a normal biliary vesicle (figs 4 and 5)

The ducts of the two bladders are histologically dissimilar throughout their entire extent and thus constitute further evidence that the struc-



Fig 4—Section through the neck of the gallbladder just distal to the valve of Heister  $\times 45$

tures are organically independent. The pancreatic duct, where it emerges from the portal lobe of the pancreas, is about the size of the choledochus but does not possess the sinus-like glands, parietal sacculi which characterize the lining of the biliary duct. In general the aberrant pancreatic duct in this case resembles normal pancreatic ducts. On entering the portal lobe of the pancreas the aberrant duct receives ductules of varying size from adjacent pancreatic lobules and empties into the main pancreatic duct which continues to the ampulla at the duodenum.

#### COMMENT AND SUMMARY

It seems assured that the relatively high incidence of pancreatic material in the porta hepatis of cats has its explanation in the hepatic



invasion of acinar tissue from the accessory lobes of the ventral pancreas during embryonic development. Although an embryonic ventral pancreas similar to that in the cat develops in the pig, as has been shown (Boyden, 1925), the manner of the subsequent development of the hepatic diverticulum and the hepatic trabeculae rather inhibits the anterior extension of these lobes into the portal area of swine. Accord-

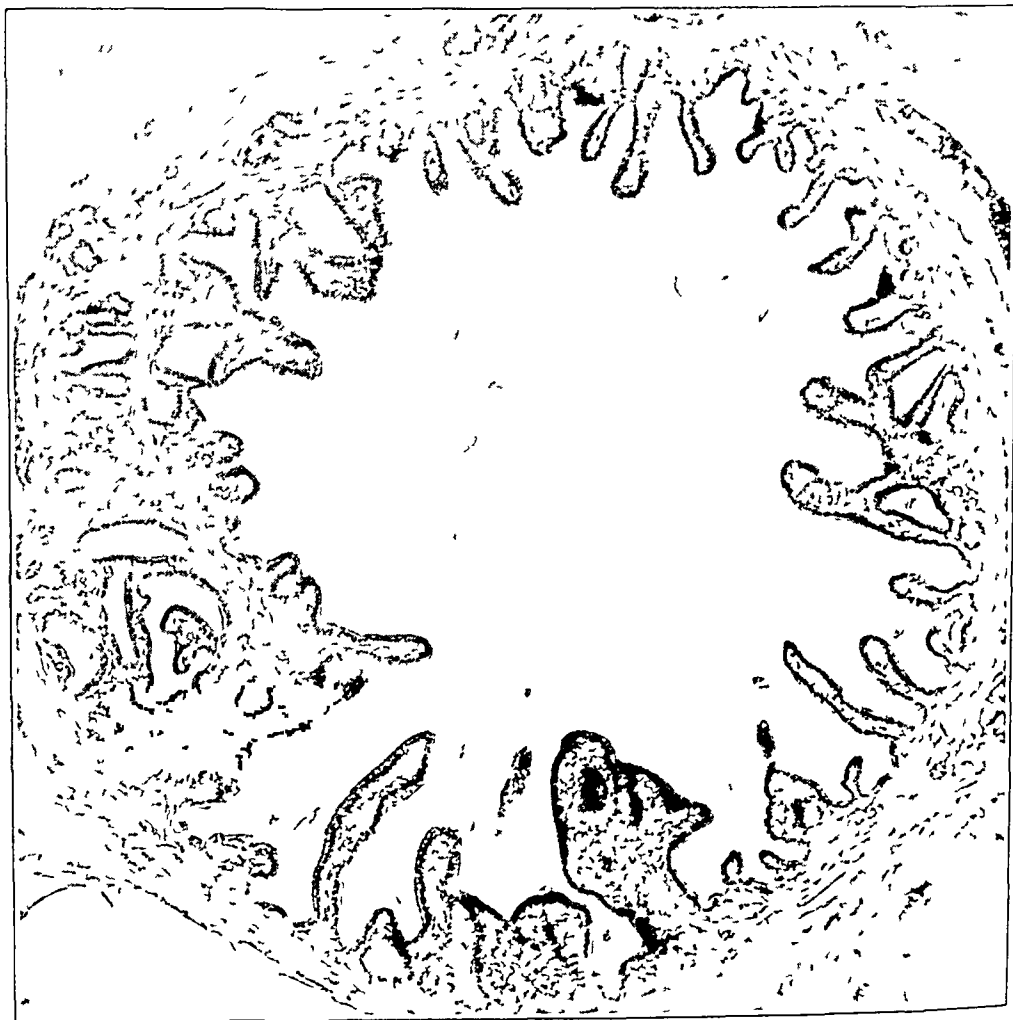


Fig 5—Section through the neck of the pancreatic bladder. The contrast between the mucosal patterns of the two vesicles is striking,  $\times 75$

ingly, accessory lobes of the pancreas rarely occur in the porta hepatis in this animal.

In many animals pancreatic tissue occurs occasionally in the hepatic area. Higgins<sup>10</sup> (1926) reported the observation in a dog of an isolated

<sup>10</sup> Higgins, G. M. An Aberrant Pancreas in the Wall of the Gallbladder of the Dog. *Anat. Rec.* 33: 149, 1926.

pancreatic lobe, buried in the wall of the gallbladder and communicating directly with the lumen of the vesicle Mann<sup>11</sup> (1920) had hitherto reported a case similar to this one, and since then has had occasion to observe another. Bowden has observed only 3 cases of pancreatic lobes reaching to the gallbladder in 2 600 sheep, and 40 such aberrant lobes appeared in the same number of cats. It seems relatively certain that it is the same type of anomaly in all animals, only more pronounced in certain ones than in others, a fact, no doubt, of embryonic significance. Just why, in certain cases, a lobe persists intact, retaining continuity with the major pancreas, entirely unrelated to the biliary tract while in others fistulous connections arise between the two resulting in complete atrophy of intervening portions of the pancreas tissue, are unanswered questions.

The various types of pancreatic anomalies in the portal region appear to fall into three groups, which are more or less indistinctly defined. The first of these involves the existence of a pancreatic lobe which extends into the portal area, frequently as far as the gallbladder, but without fistulous connections with the gallbladder or hypertrophied ducts that could function as a bladder. The second group includes those cases in which a pancreatic lobe has become attached to some part of the biliary tract, into which it continues to pour its secretions. These lobes may have arisen *in situ* or they may represent fistulous portions of a detached portal lobe. The third group of cases includes those anomalies of pancreatic organization in which the distal portion of the duct draining the ventral lobe has hypertrophied in some way to form a vesicle. Attachment to the hepatic diverticulum has carried these tissues cephalad, and they are found at various positions in the porta hepatis attached to some portion of the liver.

The various anomalies described are understood to be modifications of the same sort, and all are to be explained on the basis of embryonic development. The various cases described, in which the aberrant pancreatic ducts or bladders are confluent with biliary structures must be interpreted as the result of secondary communications between the two and not on the basis of the dual concept of the hepatic diverticulum. The histologic distinctions which maintain between the pancreatic structures on the one hand and the biliary structures on the other, which have been described and are confirmed in this study, militate against a common origin for pancreatic and biliary vesicles.

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11 Mann F C. Accessory Pancreas in the Dog. *Anat Rec* **19** 263 1920

# OCCLUSION OF THE AXILLARY ARTERY DUE TO PRESSURE BY A CRUTCH

## REPORT OF TWO CASES \*

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It is well known that the prolonged use of a crutch may induce a transitory musculospiral palsy, but damage to the main axillary vessels from the same cause appears to be an exceedingly rare phenomenon. Five years ago, a patient with obliteration of the axillary artery due to pressure by a crutch came under my observation, and several months later, a second patient was seen with an identical lesion. It was believed at first that these cases were probably unique, but later it was discovered that three similar cases had already been recorded—two by Ryle<sup>1</sup> in 1922, and one by Souques and Terris in 1924<sup>2</sup>. More recently, a fourth case has been described by Stricker<sup>3</sup> from the Strasbourg University Surgical Clinic. In view of the undoubted rarity of "crutch thrombosis," it is considered worth while to add the following cases to those already on record.

## REPORT OF CASES

**CASE 1—History**—T. K., a man, aged 38, was extremely crippled as a result of spastic paraplegia dating from early infancy (Little's disease). He had ultimately learned to walk with the aid of crutches, and in spite of his disability had worked in a useful capacity on his father's farm. Although two crutches were necessary, as a rule, he was able to progress for short distances by resting his whole weight on the left crutch only and swinging his rigid spastic lower limbs forward.

In April, 1924, he noticed for the first time a numbness in the fingers of the left hand. Two months later, owing to pain and weakness in the wrist, he consulted his physician who discovered an absence of pulsation in the radial artery. A week later, absence of pulsation was noted in the brachial artery. The pain on exertion and the sense of weakness in the limb steadily increased.

**Examination**—In July, 1924, when I saw the patient, the left upper limb was cold and abnormally pale, more especially in the forearm and hand. Pulsation was completely absent in the radial and brachial arteries, the latter vessel being palpable as a thickened cord. The subclavian and proximal part of the axillary artery showed pulsation equal to that of the opposite side. The skin of the hand

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\* From the Orthopaedic Service, Ancoats Hospital.

1 Ryle J. A. Guy's Hosp. Rep. **72** 434 (Oct.) 1922.

2 Souques and Terris. Bull. et mem. Soc. med. d. hop. de Paris **48** 536 (April 11) 1924.

3 Stricker P. Rev. de chir. **65** 617 (July) 1928.

and forearm showed no patches of duskiness or erythema, and there was no trace of edema or distention of the superficial veins. No disturbance of sensation could be demonstrated, and there was no objective evidence of paresis.

The patient was admitted to the hospital for a more complete investigation, which confirmed the absence of cardiovascular disease. A roentgen examination of the cervical spine, shoulder and upper limb revealed no bony abnormality. The Wassermann test was negative. A diagnosis of occlusion of the third part of the axillary artery due to pressure by a crutch was made, and it was assumed that a fairly satisfactory collateral circulation had been established. The patient was warned that the use of a single crutch was dangerous, and was advised to keep the limb warm, to avoid overexertion and to take great care of the skin and nails of the fingers.

*Subsequent Progress*—For various reasons the patient could not easily come to the hospital for observation, but occasional reports were received describing his progress. Writing three and a half years later he stated that he now experienced no discomfort in the hand and arm during ordinary use, but that there was an occasional ache after considerable exertion. In his opinion the skin of the limb was normal in appearance, and the limb usually felt quite warm.

*CASE 2—History*—T. A. A., a man, aged 46, had sustained an attack of poliomyelitis in early childhood. Both limbs were affected, but considerable improvement had occurred in the left leg. The right lower limb remained flail, and for many years a walking appliance had been worn. In recent years this appliance had been discarded, and a crutch on the right and a stick on the left were used instead. In walking no weight was borne on the flail limb, which merely dangled in helpless fashion. In the latter part of 1922, he became conscious of numbness and a feeling of coldness in the right hand and fingers. This gradually became more marked and later the right arm was noticed to be paler than its fellow. Ten days before the man consulted me, the arm had become very painful, especially when used.

*Examination*—In March, 1925, the right arm showed extreme pallor extending from the finger tips to the shoulder region. There was no edema and no distention of the superficial veins. On the middle and ring fingers, there were a few hemorrhagic patches in the skin over the base of the nail but no actual ulceration. The pulse was absent in the radial and brachial arteries. A feeble beat could be felt high up in the axilla but the subclavian pulse was equal to the opposite side. There were no sensory disturbances and to objective tests the strength of the hand and forearm seemed undiminished. A diagnosis of occlusion of the right axillary artery due to pressure by a crutch was made. The patient was urged to discard his crutch and to attempt weight bearing on the flail limb with the aid of a splint. The usual precautions for the care of the hand were emphasized.

*Subsequent Progress*—When the patient was examined two years later, the hand and arm were found to show a much better color, and the limb could be used freely without discomfort.

#### COMMENT

In the cases observed by Ryle and by Souques and Terris the condition of the affected limb at a later date is not recorded. Stricker's case is notable, owing to the development of gangrene in the fingers, a complication that was treated by arteriectomy (Leriche<sup>4</sup>). There are several points of considerable interest in the clinical picture of thrombo-

<sup>4</sup> Leriche and Stricker. *P. Brit. I. Surg.* 16: 63 (Jan.) 1929.

arteritis caused by pressure from a crutch. In the first place, the absence of any sign of venous compression is remarkable, for it is well recognized that primary thrombosis of the axillary vein may be produced by a comparatively trivial injury. Gould and Patey,<sup>5</sup> who have recorded eight cases of this unusual vascular lesion, suggested that the thrombosis is the result of the rupture of a delicate valve by pressure of the subclavius muscle when the vein is distended during expiration. How the axillary vein escapes damage from pressure by the crutch is thus not easy to explain.

It is evident that arterial occlusion from pressure by a crutch is ordinarily a gradual process which gives ample time for the development of an efficient collateral circulation. Until compensation is fully established, the subjective and objective symptoms of ischemia (pain on exertion, paresthesia, etc.) are well marked, and for a time there is a risk that trophic ulceration or gangrene may follow. But if the affected limb is protected from further injury and overexertion is avoided, there is every prospect that little or no impairment of function or nutrition will ultimately be demonstrable. This sequence of events is well illustrated in the two cases which form the subject of this paper.

It is further necessary to emphasize the dangers that attend the prolonged use of the ordinary type of axillary crutch, and particularly when the whole body weight is borne by a single crutch. The more careful fitting of crutches in general and the adoption of the "elbow" pattern have undoubtedly made crutch palsy increasingly unfamiliar. These precautions will also tend to minimize the risk of the more serious vascular lesion. Persons with severe residual paralysis of the lower limbs should be provided with efficient walking appliances, and taught to use one or two sticks. The dangling leg and single crutch should never be countenanced.

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5 Gould, E. Pearce, and Patey, D. H. *Brit J Surg* 16:62 (Oct) 1928.

# SUPPURATION IN THE SUBPHRENIC REGION

WITH SPECIAL REFERENCE TO PRIMARY IDIOPATHIC LIVER AND  
SUBPHRENIC ABSCESS \*

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For the purposes of this paper, owing to the similarity in the clinical manifestations of subphrenic and nonamebic liver abscess, these two conditions are considered together, an additional reason being that they are often associated in the same patient and their surgical management is identical

Any localized collection of pus in contact with the undersurface of the diaphragm is considered by Barnard<sup>1</sup> as a subphrenic abscess. He also included any liver abscess which is near the surface and more or less intimately associated with the diaphragm. This designation appears proper in view of the similarity of the clinical features as presented in the cases of both liver and subphrenic abscess. This similarity is so great in many of the cases as to make a differential diagnosis either difficult or impossible.

A suppurative process in the subphrenic space and liver occurs under a variety of circumstances. Infection usually reaches the subphrenic regions by direct extension or through the lymphatics in such acute abdominal conditions as perforated gastric or duodenal ulcers, acute appendicitis and following operations on the biliary tract. A collection of purulent exudate under the diaphragm, most commonly the right half, is not an uncommon postmortem observation in patients who have died of a diffuse peritonitis of appendical origin or peritonitis from other sources. Patients who recover from a serious peritoneal involvement may at some subsequent time have an abscess in the subphrenic space.

A retrocecal gangrenous appendix may involve the subphrenic area by extension of its infection along the retroperitoneal cellular tissue.

I have found large collections of purulent exudate in the left subphrenic space in two fatal cases of perforated gastric carcinoma and in two others with suppurative lesions of the spleen.

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\* Submitted for publication Sept. 3, 1929.

\* Read before the Bronx Surgical Society, April 22, 1929.

\* From the Surgical Services of Drs. Henry Roth and L. Miller Kahn.

1. Barnard H. L. Brit. M. J. 1:371, 1908.

Infections in the kidney less commonly give rise to subphrenic abscess. An empyema thoracis is rarely complicated by a subphrenic abscess. In approximately 150 consecutive cases of empyema, I have never observed this complication, nor have I ever discovered it post mortem in fatal cases of empyema.

Beye<sup>2</sup> studied 190 cases of empyema with this association in mind and found one case in which trauma to the diaphragm during operation was probably responsible.

Whipple,<sup>3</sup> in studying 1,000 cases of subphrenic abscess, found that 25 per cent were due to lesions of the stomach, 21 per cent of the appendix, 16 per cent of the biliary tract and 5 per cent of the duodenum, the rest being secondary to lesions of the kidney, spleen, pancreas and lungs.

The liver may become infected from several sources, the avenue of infection being the blood stream or the portal system. Any infective lesion in the gastro-intestinal tract may give rise to liver suppuration, the most common being acute appendicitis. Septic material is transported from a thrombophlebitis of the mesentery of the appendix through the portal vein to lodge in the portal branches where it causes the well known clinical lesion, pylephlebitis. This complicates from 0.1 to 0.4 per cent of all cases of acute appendicitis. In one of my cases pylephlebitis complicated suppurative mesenteric glands. Tropical dysentery is well known as a forerunner of amebic solitary abscess of the liver.

Multiple small hematogenous liver abscesses are not infrequently seen post mortem as part of a grave general infection of the blood stream.

Any septic focus in the body may give rise to a hematogenous transport of a septic embolus with localization in the liver where it may form a solitary liver abscess. One liver abscess of that type developed in a patient with a lung abscess.

Long-standing infection in the common bile duct not infrequently causes an ascending biliary infection, suppurative cholangitis and multiple cholangitic liver abscesses.

Large penetrating peptic ulcers attached to the liver have given rise to suppuration of the liver.

In my cases trauma has not exerted any influence in their development.

Five of the cases reported in this paper were liver abscesses and three subphrenic of the primary idiopathic type differing from those

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<sup>2</sup> Beye H. L. Subphrenic Infection. Report of Ten Cases, *Arch Surg* 14 240 (Jan) 1927.

<sup>3</sup> Whipple, M. O. *Am J Surg* 40 1, 1926.

alluded to in the foregoing general discussion in that no etiologic basis was found for their existence

No clinical or postmortem observations were discovered which could be held responsible

There was no history of biliary disease, appendicitis or any other intra-abdominal lesion. There was no history of dysentery, and evidence of it could not be demonstrated. Amebas were not found in the pus or in the scrapings from the abscess wall.

It appears likely that some cryptogenic infection gave rise to a hematogenous transport of septic material which localized in the liver or subphrenic space.

#### PATHOLOGY

The type of lesion produced varies with the nature of the primary lesion. In pylephlebitis the liver is large and swollen and on section may show small thrombi in the portal branches or distinct suppuration. If the condition is advanced, there may be liver destruction with multiple coalescent abscesses. If the suppuration is secondary to infected bile passages, the liver is also large, swollen and greenish, and on section the bile channels are found to be distended with a greenish purulent exudate. The end-result is multiple cholangitic abscesses.

In the multiple hematogenous abscesses, the liver is swollen and is the seat of many small scattered abscesses such as those found in the other organs in grave general infection.

The liver abscesses in five cases presented here were large, single and situated in the right lobe of the liver near the surface. In two it was multilocular and at first gave the impression that they might have been multiple. The abscess wall was unusually thickened and grayish. The content of the abscess was a greenish, purulent exudate varying from 250 to 1,500 cc. The abscesses appeared as if they had existed for a long period. The liver was much enlarged, and the capsule was thickened, especially that part overlying the abscess. In four of the cases the abscess perforated into the subphrenic space and formed what may properly be called a "subphrenic-hepatic" abscess. In case 5 it perforated the diaphragm and formed a circumscribed abscess between the lower lobe of the lung and the liver. In cases 7 and 8 the abscess was breaking through the lateral chest wall in the lower part. The liver may be intimately associated with the diaphragm and firmly attached to the chest wall, as was present in case 7.

In the primary idiopathic subphrenic abscess, as in the secondary, it may be situated in any one of the six anatomic regions of the subphrenic space described by Barnard. These spaces are right and left anterior intraperitoneal, right and left posterior intraperitoneal and right and left extraperitoneal. The abscesses are usually large and sur-



rounded by a zone of marked inflammatory reaction. In cases coming to autopsy, there was a variety of pathologic changes in the lungs, such as marked fibrosis and moderate dilatation of the bronchioles, especially in the lung corresponding to the side of the subphrenic lesion. Areas of bronchopneumonia and bilateral pulmonary furuncles were seen. The latter were undoubtedly caused by extension from the local seat along the lymphatics or blood stream.

The organisms most commonly found were streptococcus, staphylococcus and colon bacillus. In the secondary type anaerobes are frequently found. In those of my cases in which pleural fluid was aspirated it was found to be clear and straw-colored and revealed the presence of gram-positive and gram-negative organisms on smear but failed to grow when cultured. These organisms were probably attenuated by the bactericidal properties of the same.

#### CLINICAL AND DIAGNOSTIC FEATURES

Any patient who has had an acute intra-abdominal infection may develop secondary subphrenic or liver suppuration and should be watched carefully for the signs and symptoms of the same.

The secondary subphrenic and liver abscess lends itself more readily to early recognition, especially if the primary condition has recently preceded it. A patient may reasonably be suspected of having pylephlebitis if subsequent to an operation for acute appendicitis he suddenly runs a septic temperature with chills, sweats and jaundice and has bile in the urine and tenderness over a large liver. The knowledge that such a primary condition not infrequently gives rise to this complication should offer a clue for a search and early recognition. The symptoms of this complication may appear from a few days to several months after the antecedent primary infection. This antecedent disorder may be forgotten or even appear irrelevant to those unfamiliar with the symptoms of this complication.

When a secondary liver abscess or subphrenic abscess develops, the clinical features are similar to the primary idiopathic subphrenic lesion. The primary idiopathic subphrenic and liver abscess or a combination of both offers greater difficulty in their detection because no antecedent lesion is present to offer some clue. A liver abscess constituted an unexpected observation at autopsy in one of my cases in which it was not even suspected.

The onset in the eight primary cases reported here was slow and insidious. There was generalized pain sometimes localized to the chest, an elevated temperature, chilly sensation and a slight cough. Grip was the condition thought to be present in every case by the physician in attendance. After a short period of advised rest, temporary improvement followed. The patients continued in a state of ill health, with

malaise, increasing weakness and elevation in temperature. When the clinical features assumed a more serious aspect, they were referred to the hospital. Pain was the outstanding symptom and was usually located on the side corresponding to the lesion, sometimes in the right or left upper quadrant, in the costal margin or in the lower part of the chest posteriorly. At times the pain was sticking and referred to the right shoulder or to the left in a left subphrenic lesion.

Pain was most pronounced when perihepatitis was most marked. There was a slight cough, usually nonproductive, rusty sputum was never present, jaundice was present in one case. It is more common in pyelephlebitis and cholangitic abscesses. It usually draws one's attention immediately to the liver, and in case 4 it was of considerable aid in the prompt recognition of the liver abscess.

Tenderness of varying degree is always present if the lesion has existed for some time.

The patient in case 4 presented marked tenderness and some rigidity in the right upper quadrant. It may sometimes best be elicited by anteroposterior or lateral compression of the lower part of the chest wall. A sense of fulness or a mass and even fluctuation may be detected.

The liver was markedly enlarged in one case in which it was palpated five fingerbreadths below the costal margin. In liver abscesses the liver is usually enlarged, but failure to palpate it may be caused by the fact that the enlargement takes place under the diaphragm, which it pushes upward. When palpated, however, it can be felt below the free border of the ribs.

Edema over the lower axillary part of the chest on the side of the abscess was present in four cases. It generally appears when the lesion is well advanced, and is absolutely characteristic and positive evidence of a subphrenic abscess or a liver abscess which had perforated into the subphrenic space. This sign cannot be depended on in the early diagnosis, as it appears late in the disease.

Examination of the chest revealed various signs such as râles, dullness to flatness, bronchial breathing and diminished fremitus, all of which led to an admission diagnosis of pneumonia or pleurisy with effusion in every case. Eliason<sup>4</sup> reported such diagnostic error in fourteen cases of liver suppuration before a correct diagnosis was arrived at. Pancoast<sup>5</sup> also admitted errors of such nature prior to his familiarity with the roentgen evidence of subphrenic suppuration.

The secondary changes in the chest were so predominant at first as to overshadow completely the exact nature of the lesion, which was not

4 Eliason E. L. Surg. Gynec. Obst. **42**: 510, 1926.

5 Pancoast H. K. Am. J. Roentgenol. **16**: 303, 1926.

revealed until the roentgen examination and fluoroscope presented the evidence which is now known to be characteristic of a subphrenic or liver abscess. Until then the roentgen ray confirmed the clinical opinion of a condition of the chest.

The roentgen features of a liver or subphrenic abscess are elevation of the diaphragm and limitation in excursion. The height of the diaphragm varies with the location of the abscess and with its nearness to the dome of the diaphragm.

In case 1 the roentgen signs appeared late because the abscess evidently began low down near the diaphragmatic attachment and reached the dome when the abscess was well advanced. In case 7 the elevation of the diaphragm was slight, because the abscess was perforating externally through the chest wall and away from the dome.

Restricted motion also depends on the extent of the pathologic change. It is more marked in subphrenic than in liver abscess because there is usually greater inflammatory reaction in the former which binds it to the chest wall. In case 4 the lesion was thought to be in the liver, because there was free excursion although the diaphragm was distinctly elevated.

Two cases showed the presence of air with a fluid level below the diaphragm.

It cannot be emphasized too strongly that roentgen examination should be repeated frequently whenever such a lesion is believed to be developing.

Constitutional symptoms were pronounced and became progressively worse until the abscess was drained or until death occurred.

The temperature usually ranged between 100 and 103 F. with an elevation of from 105 to 106 F. The course did not resemble that seen in pyelphlebitis except in case 4. If the abscess was well encapsulated, the temperature was of low grade.

Chills or chilly sensation were common. Sweating was a constant and troublesome symptom, in the advanced cases there was profound debility and marked emaciation.

The examination of the blood showed a white count ranging between 13,000 and 28,000 with a high differential count. A marked secondary anemia was present in some cases, necessitating transfusion. The entire attitude was one of great anxiety and grave illness.

A diagnostic puncture of the subphrenic space or liver is advised by some although it appears to be a highly dangerous procedure with little advantage to the patient. It should never be done outside of the operating room, where one should be prepared for immediate operation.

In any case in which one has reason to suspect such a condition it is far safer to explore this territory under local anesthesia in order to establish its presence or absence. Direct palpation and visualization

through this incision will usually yield sufficient information to guide one in the further management of the case

Case 1 prompted this plan in the absence of more definite evidence. Through a left lumbar oblique incision suggestive pathologic changes in the kidney and perinephric space were excluded. The left extra-peritoneal subphrenic space was explored, and a large, apparently inflammatory mass was discovered. The discovery of the mass led to the location of the abscess. Pus even then was obtained with great difficulty and only after several punctures in different areas under direct visualization, but at least it was obtained without danger of infecting foreign territory. In case 6 diagnostic puncture resulted in infection of the pleural cavity which later necessitated an operation for empyema.

#### TREATMENT

The secondary subphrenic and liver abscess may be prevented in certain cases if one is familiar with the variety of conditions which are responsible. Prompt recognition and proper management of these preceding intra-abdominal infections preclude the spread of infective material along any of the avenues which reach the liver or subphrenic space, when the complication does occur, the management is the same as in primary abscess.

Early recognition and timely operative intervention should be the aim of every surgeon and clinician, lest fatal secondary pathologic changes ensue.

Supportive measures should be instituted as early as possible. Transfusions are highly beneficial for patients with secondary anemia. Large quantities of 5 per cent dextrose injected intravenously are especially indicated. When the patient is so poor an operative risk, such preoperative therapeutic measures often tide him over the shock incident to even so slight an operation.

The method of approaching the abscess cannot be governed by any rules as each case is individual. The choice of approach should depend as it did in my cases, on the location of the abscess as indicated by the signs and symptoms. I have chosen either the anterior or posterior route or the combined routes whenever it appeared that adequate drainage would be best secured. Contamination of the pleural and peritoneal cavities is the great danger one must guard against. When feasible a two-stage operation is advisable to insure the formation of adhesions about the liver or subphrenic space, thereby excluding it from the pleural and peritoneal cavity. When this field is properly isolated the abscess is opened and drained. Thorough drainage is essential. This may not only be enhanced by the proper use of the aspirator at the time of operation but may be repeated in bed. This procedure was carried out in case 4. Supportive treatment should be continued until the patient is well advanced toward recovery from this prolonged illness.

## MORTALITY

The outcome depends on several factors the extent and location of the abscess, its duration and the extent of secondary pathologic changes, which alone may be sufficient to terminate life. A pyelephlebitis is invariably fatal, multiple liver abscesses and an undrained liver or subphrenic abscess are usually fatal. According to Lockwood,<sup>6</sup> in the cases in which operations are performed, the mortality rate varies between 20 and 50 per cent. In the primary type, it seems that the mortality rate is apt to be greater, because it is slightly more difficult to recognize. One of the three patients with a primary subphrenic abscess died without having been operated on. Three of the five patients with abscess of the liver died, two were operated on several times, but for secondary collections of pus apparently remote from the huge primary liver abscess which was undiscovered until after death, the third died of a diffuse peritonitis as a result of leakage of pus into the peritoneal cavity.

It is well known that spontaneous rupture of a subphrenic abscess may occur into almost any adjacent organ or space. In one, it perforated into the pleura, resulting in almost immediate death, another ruptured into a bronchus, in two, it was breaking through the chest wall and appeared in the lower part of the axilla as a fluctuating area. Spontaneous rupture may occur into any hollow organ, where spontaneous cure may result.

In one case reported here (case 7) and in another case of secondary subphrenic abscess following acute appendicitis, the pus gravitated to the perinephric region and gave the clinical signs of a perinephric abscess. Incision and drainage of the perinephric abscess did not result in a cure in the latter case until at a second operation a sinus tract was traced to the right subphrenic space, where a huge collection of pus was drained, rapid recovery then took place. The patient in my case 7 was not so fortunate.

## COMMENT

Objection might be made to the terminology of primary liver or subphrenic abscess as applied to the eight cases reported in this paper. I have tried to avoid this designation, but because of the absence of any evidence of the usual causative factors I feel justified in this decision.

In case 1 the patient had a severe pyuria, the source of which could not be determined, the kidney corresponding to the side of the abscess showed no gross pathologic change. The association of the pyuria and subphrenic abscess is purely speculative. The patient in case 6 had an empyema thoracis subphrenic and liver abscess. One might argue in

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6 Lockwood A L Surg Gynec Obst 33 502 1921

tavor of a diagnosis of primary empyema with the other lesions secondary, the facts favor the reverse

The patient in case 4 gave a history of jaundice and pain in the right upper quadrant one year before, which lasted for only one week. This is strongly suggestive that some biliary infection was present which recurred at the present time leading to a liver abscess.

That some obscure undiscovered gastro-intestinal lesion was present cannot be affirmed. It is not unlikely that some form of infection, known commonly as grip, was present, but no causal relation could be established.

One might interpret the changes in the lung as real pneumonia and a primary source of the subphrenic lesion. I can say with almost absolute certainty that the lung is compressed by the elevated diaphragm and the plural fluid. The latter changes promptly disappear after the abscess is drained and the diaphragm returns to its normal position. If extension takes place from the lung to the subphrenic region, one would have to imagine a retrograde lymph flow.

#### CONCLUSIONS

1. Liver and subphrenic abscesses arise without demonstrable foci of infection, thus constituting the primary and idiopathic type.

2. The recognition of this condition is usually late, when it is well advanced.

3. The condition is most commonly mistaken for pneumonia or pleurisy with effusion.

4. The roentgenograms and fluoroscopy aid in disclosing the lesions.

5. The roentgen features are (a) an elevation of the diaphragm with restricted excursion, (b) the presence of air with or without a fluid level beneath the diaphragm and (c) intrathoracic changes leading to a diagnosis of pneumonia and pleural effusion.

6. The mortality rate is high because the condition is either not recognized at all or is recognized so late that extensive associated pathologic changes have taken place or because the abscess is inadequately drained. In the patients in whom the cases were recognized early and who were operated on promptly the mortality rate was greatly reduced.

#### REPORT OF CASES

CASE 1.—P. R., a man aged 47, was first seen by me on May 3, 1928, because of mild pain in the suprapubic region of three days' duration and unassociated with other symptoms. Physical examination failed to reveal evidence of abdominal disease. There was a moderate number of pus cells in the urine, the prostate was not enlarged and a marked phimosis was present. The following day there was slight difficulty in voiding; the number of pus cells in the urine had increased. Roentgen examination of the genito-urinary tract failed to reveal any evidence

of calculi. On the following day, a circumcision was done so that a cystoscope could later be introduced to study the urinary tract. The wound was healed in ten days. Frequency of urination, dysuria, pyuria and a rise in temperature continued for several days, there was no abdominal or kidney tenderness. Sore throat, generalized pain and chilly sensations developed, in other words, a condition that proved to be a grip infection. The patient looked septic, and was advised to enter the hospital on May 21. On admission, the temperature was 103 F, respirations 23 and pulse rate 100. In the right side of the chest posteriorly at the base, a few subcrepitant râles were heard, and later signs of lobar pneumonia developed. The abdomen was soft but not tender. No masses were felt. The blood showed white blood cells, 12,000, polymorphonuclears, 76 per cent, and lymphocytes, 24 per cent. The urine had large amounts of pus clumps. A Widal test, chemical analysis of the blood and blood culture gave negative results. In ten days, the pneumonia of the right lower lobe had resolved almost completely, and the left lower lobe was involved, this was confirmed by the roentgen ray. Cough was slight, with little expectoration, the sputum did not show tubercle bacilli and was negative for types 1, 2 and 3 pneumococcus. The hemoglobin was reduced to 55 per cent, the white blood cells were now 18,400 with a high differential count.

The patient looked profoundly septic. A transfusion of 300 cc of citrated blood was given in bed. Signs in the left side of the chest continued for about two weeks, at which time fluid was thought to be present in the pleural cavity. There was now pain in the left lumbar region, with marked left costovertebral tenderness. Roentgen examination of the chest showed an unresolved pneumonia with some fluid on the left side. On fluoroscopy, the diaphragm moved freely on both sides. The course was still septic, there were profound weakness and anemia, the hemoglobin was down to 42 per cent, sweating was profuse and constant, and emaciation was marked. Another transfusion of 450 cc of whole blood was given. About six weeks after admission, a tap of the left side of the chest resulted in 30 cc of clear straw-colored fluid which contained gram-positive cocci that failed to grow on culture, tubercle bacilli were not present. Blood culture was sterile. About two months after admission, there was slight bulging and edema over the lower part of the left side of the chest in the postaxillary part. This sign was persistent and seemed to favor a previous clinical impression that a subphrenic abscess existed and that the changes in the left side of the chest were secondary. Within the following week, 35 cc more of clear straw-colored fluid was aspirated from the left side of the chest. Repeated roentgen examination and fluoroscopy showed unresolved pneumonia with pleuritis and moderate pleural effusion. Exploration of the left subphrenic space was considered mainly on the clinical features, but this procedure appeared somewhat too radical without the usual roentgenologic evidence which was familiar to me. About two days before the operation, the last roentgen examination and fluoroscopy revealed the left half of the diaphragm to be slightly more elevated and restricted in excursion. Another transfusion was given. Operation was undertaken on July 31, about ten weeks after the patient's admission to the hospital. An incision was made over the left kidney, because it appeared as if a perinephric abscess might be present which extended to the under surface of the diaphragm. The left kidney and perinephric space were found lacking in gross evidence of disease. When the hand was insinuated upward toward the diaphragm, a large mass was discovered which was obviously inflammatory. Pus was obtained after several punctures, the abscess was opened and drained. The pus yielded *Bacillus coli* on smear and culture. There was considerable postoperative shock for twenty-

four hours, but following that convalescence was uneventful. The patient was discharged twenty-four days after the operation. The drain had been removed a long time before and the wound was almost entirely healed. He is now well. It may be of interest to mention that the pathologic changes in the chest disappeared almost entirely a few days after the operation.

CASE 2—A S, a woman, aged 44, was admitted to the hospital in March, 1927, with pain in the left side of the chest and elevation in temperature. The present trouble began five weeks previously with sore throat, fever and malaise. She was told that she had grip and was advised to stay in bed for a few days, temporary improvement followed. Three weeks before admission the symptoms recurred, but were more aggravated. Pain was sticking in character and more marked on inspiration, there were chilly sensations, a slight cough and fever. Her previous history was unimportant except for pneumonia six years before, and diabetes was present for seven years.

On admission she looked acutely ill and slightly cyanotic. The lower part of the left side of the chest was sensitive to anteroposterior compression. There was also a small area of bronchovesicular breathing over the base of the left lung, with an increase in transmission of spoken and whispered voice. The abdomen was tender in the left subcostal region, and the muscles were spastic but not rigid, there was tenderness over the left kidney as elicited by first percussion.

The temperature ranged between 99 and 102 F throughout the entire course. The white blood count was 16,800, with a differential count of 84 per cent polymorphonuclears and 12 per cent lymphocytes, the red blood count was 3,800,000. The urine showed a moderate number of white cells. More tenderness gradually developed in the left upper quadrant, also a mass which at first gave the impression that it was a kidney mass. The latter being excluded by cystoscopy and roentgen examination, a left subphrenic abscess was strongly considered. This mass grew larger and nearer to the ensiform, where it showed fluctuation. Roentgen examination five days after admission showed no gross changes in the lungs, the left half of the diaphragm was higher than normal. At a later examination, the stomach showed no evidence of an organic lesion.

Four weeks after admission a large left subphrenic abscess was drained through an incision over the fluctuating area. *Staphylococcus aureus* was cultured from the pus. The patient made an uneventful recovery and was discharged nine days later with a small sinus.

CASE 3—A R, a man, aged 35, was admitted to the hospital in April, 1926, with severe pain in the right side of the chest and fever. The onset of the present illness was four months before, when he noticed that he tired easily, had pains in the limbs and a slight rise in temperature varying between 100 and 102 F. He was told that he had grip, so he rested for several days. Three weeks before admission, he developed pain in the right side of the chest which was aggravated on inspiration, the pain radiated to the right shoulder. One week before admission the temperature began to run a septic course, he perspired freely and became very weak, there was no cough or bloody expectoration. A roentgenogram of the chest before admission failed to reveal any changes in the lungs.

On examination, although he seemed well developed, he had lost weight, he perspired profusely. The right side of the chest was dull at the base anteriorly and posteriorly, there was diminished breathing, no rales were present. The heart was pushed slightly to the left. The abdomen was soft, not tender, there was some pain on anteroposterior compression of the lower right side of the chest.



The temperature was 104 F., the pulse rate was very rapid, and respiration at times was rapid. The blood showed 20,000 white cells, with a differential count of 82 per cent polymorphonuclears and 18 per cent lymphocytes. The condition was regarded as pleurisy with effusion. On aspiration, 260 cc of clear serous straw-colored fluid was obtained from the right side of the chest which showed no organisms on smear or culture and no tubercle bacilli. Bronchial breathing was heard after the chest was tapped. Slight tenderness developed in the right upper quadrant. A few days later, the chest was tapped again and 15 cc of similar fluid was obtained.

Five days after admission, roentgen examination revealed the right half of the diaphragm to be higher than normal. Fluoroscopy showed diminished excursion, there was also a small air pocket below the diaphragm. The roentgenologist's opinion was that there was a lesion below the right half of the diaphragm, probably an abscess.

Two weeks after admission, a roentgenogram confirmed the previous report and revealed a dense homogeneous shadow in the right basal region, which was interpreted as pleural effusion.

The clinical course was distinctly septic, the patient was progressively getting worse, weakness was extreme, and profuse perspiration was constant. He suddenly went into collapse, his pulse became very rapid, almost imperceptible, there was marked cyanosis, rales were heard over the entire chest. Death followed. Immediately after death, aspiration of the chest revealed seropurulent fluid.

The subphrenic space was also punctured, and 250 cc of purulent exudate was obtained. Autopsy was refused. It appears likely that the subphrenic abscess perforated into the right pleural cavity causing almost sudden death. At this time, the pleural fluid did not show any organism on smear or culture. Guercup inoculation failed to show evidence of tuberculosis. Through some error, the subphrenic exudate was not examined bacteriologically.

**CASE 4**—C. L., a man, aged 40, was admitted to the hospital in February, 1929. Three weeks before, he suddenly experienced a sharp, sticking pain in the right upper quadrant. He had some fever and a slight cough. His condition was thought to be influenza, so he was advised to stay in bed for one week, after which he improved. He left the city for two weeks, but when he returned the rise in temperature and cough returned. Jaundice had also developed. His past history was unimportant, except that he believed that he had had a similar condition about one and one-half years before, which lasted for only one week, after which he had felt well until the present time.

On entrance to the hospital, he looked acutely ill and was moderately jaundiced. There were fine crackling rales at the right base posteriorly, breath sounds were diminished, the left side showed no change. The abdomen revealed a large liver reaching five fingerbreadths below the costal margin, marked tenderness was present in the right upper quadrant and also in the right costovertebral angle. The urine did not show any change. The temperature was 104 F., respiration, 25, and the white blood count 16,800, with a differential count of 88 per cent polymorphonuclears and 12 per cent lymphocytes. On admission a diagnosis of pneumonia was made first, then a provisional diagnosis of subphrenic or liver abscess was promptly made, and was confirmed by the roentgen ray and fluoroscopy.

The roentgen examination disclosed infiltration at the right base, the right half of the diaphragm was slightly higher than normal, below the diaphragm was seen air with a fluid level, diaphragmatic excursion was slightly restricted. The

conclusion was that an abscess of the liver was present, although a subphrenic abscess could not be excluded.

Immediate exploration through an incision in the right upper quadrant disclosed a large abscess in the liver when it was punctured. The needle was left in situ and the liver was packed all around to wall it off from the peritoneal cavity, forty-eight hours later, the abscess was opened and drained, 1,500 cc of pus was obtained by suction. For three days following the operation the patient's course was septic, but thereafter he made an uneventful recovery and was discharged thirty-five days later.

CASE 5—A B, a man, aged 30, was admitted to the hospital in December, 1927, complaining of sore throat, pain in the chest and back and chilly sensations and fever, all of which began six days before. A physician diagnosed his condition as grip. After a short rest in bed, he improved. Shortly after he experienced a tired feeling, pain in the chest and chilly sensations, he perspired freely. It was believed that pneumonia was developing. When he entered the hospital he looked acutely sick. Over the right side of the chest posteriorly there was diminished tactile and vocal fremitus. There was flatness to percussion at the right base, and no rales, breath sounds were distant and bronchovesicular. The abdomen was soft, not tender or rigid in any part.

The diagnosis was pleurisy with effusion.

The temperature was 102 F, respiration, 22, and pulse rate, 100, the urine showed a trace of albumin, a few granular casts and a moderate number of white blood cells, the blood count was 14,000, with a differential count of 85 per cent polymorphonuclears and 15 per cent lymphocytes. The patient's course continued septic. The blood culture was sterile. A roentgenogram of the chest five days after admission failed to reveal any gross changes in the lungs. Twelve days after admission, 50 cc of clear, straw-colored fluid was aspirated from the right side of the chest, no organism was obtained on culture of this fluid. Of the cells present, 95 per cent were polymorphonuclears and 5 per cent lymphocytes.

Another roentgenogram taken seventeen days after admission showed a homogeneous shadow in the right side of the chest from the sixth rib down, merging with a slightly elevated diaphragm. The diaphragm moved freely. The roentgen observations suggested a lesion below the diaphragm, probably in the liver, because of free excursions of the diaphragm.

The following day the ninth rib in the postaxillary region was resected, the pleura was pushed away from the diaphragm and a liver abscess was opened and drained, the pus contained nonhemolytic streptococci. The following day the abdomen was markedly distended and tender, more markedly in the lower quadrant. The abdomen was opened, because an intraperitoneal infection was suspected, no exudate was found. The old abscess was explored through the old incision, and then an incision parallel to the right costal margin was made. A large quantity of pus was evacuated. The patient's condition was desperate, the pulse was very weak and rapid, the temperature was 106 F, death ensued the following day.

At autopsy, a large multilocular abscess was found in the right lobe of the liver. This had perforated into the subphrenic space and then through the diaphragm to form a localized collection of pus under the right lobe of the lung. The right lung was compressed at the base. Both lungs contained many small abscesses. There was a diffuse peritonitis due to leakage of pus from the liver abscess along the right lumbar gutter, where most of the exudate was found.

CASE 6—K B, a man aged 47, was admitted in September 1926 complaining of pain in the right side of the chest and fever which had developed thirteen days

before after exposure to rain. He was compelled to remain in bed for a few days on account of marked weakness and chills.

On admission, he looked acutely ill. The temperature was 101 F, and respiration, 35. Over the right base posteriorly there were flatness, diminished tactile fremitus and distant tubular breathing. In the right upper abdominal quadrant, tenderness and slight resistance were present, the white count was 13,000, with 88 per cent polymorphonuclears and 12 per cent lymphocytes. A tentative diagnosis of pneumonia with pleural effusion was made. The chest was tapped, and purulent exudate was obtained at the eighth interspace. The following day, part of the eighth rib was resected for what appeared to be empyema, some purulent exudate was obtained. The patient's course remained septic with the temperature ranging between 101 and 103 F, sometimes higher. The pus from the empyema showed gram-positive cocci on smear, but no growth on culture. It was negative for pneumococcus types 1, 2 and 3. A chemical analysis of the blood and urinalysis gave negative results.

Two weeks after admission, a roentgenogram of the chest disclosed the right half of the diaphragm higher than normal, and the fluoroscope showed diminished excursion, these observations suggested a lesion below the diaphragm. In the right upper quadrant, a tender, bulging mass developed which was thought to be an abscess of the liver. On September 22, an abscess of the liver was drained through a right upper rectus incision. Three weeks later, a subphrenic abscess was drained through the old incision. The pus from the abscess of the liver was sterile. *Staphylococcus aureus* was obtained from the subphrenic abscess. The patient made an uneventful recovery after the last operation, and was discharged on November 9.

It seems more likely that a primary abscess of the liver was at first present, which perforated into the subphrenic space and then subsequently infected the pleural effusion, causing empyema.

CASE 7—H. K., a woman, aged 27, came to the hospital on July 7, 1924, with pain in the right costal margin and fever. She had pneumonia three months before and remained in bed for ten weeks. Since then she had pain in the right side of the chest posteriorly and in the right costal margin, it had been much worse for the past five weeks, she had lost weight and had become considerably weakened.

When she entered the hospital, she appeared pale and had a few fine râles at the right base posteriorly. There was tenderness of the right costal margin and the lower part of the right side of the chest posteriorly, which was best elicited by anteroposterior compression of the right side of the chest.

The temperature was 102 F, the pulse rate 90, and respiration, 20, hemoglobin was 66 per cent, and the white blood count was 16,200. The urine was normal. The chemical analysis of the blood gave negative results. A few days after admission, there was tenderness in the right loin and costovertebral angle. A perinephric abscess was suspected. Cystoscopy and roentgenography failed to reveal any evidence of pathologic changes in the genito-urinary tract.

Two weeks after admission, an area of induration and fluctuation, 3 inches (7.6 cm) in diameter developed, which was apparently adherent to the tenth to the twelfth ribs in the right axillary region, a puncture in this area failed to reveal pus. A roentgenogram of the chest at this time showed a few fine infiltrations in the right base from the seventh rib to the diaphragm, there were no gross changes in the left lung. The right half of the diaphragm was limited in excursion.

An incision over this indurated area over the right side of the chest revealed the presence of pus, probably an abscess of the chest wall. The pus showed no

organisms on smear or culture. The discharge gradually diminished, and a small sinus remained. Five weeks later, induration developed about the sinus, so further exploration was done, the tenth rib was resected for about 2 inches (5 cm). A small amount of purulent exudate was again drained. Healing had again resulted in a persistent fistula. The pus was sterile, no tubercle bacilli were found and no evidence of actinomycosis. The patient was discharged on Nov. 12, 1924, with a sinus in the lower right side of the chest region which was persistent. She returned on Jan. 12, 1925, when the sinus was again explored and found leading downward anteriorly to the pleura, where a small collection of purulent exudate was discovered. *Staphylococcus aureus* was now present in the pus. There was no evidence of malignancy. The Wassermann reaction was negative. Roentgen examination of the chest showed partial obliteration of the right costophrenic sinus with a few fine infiltrations in the right lung. The ribs did not show evidence of osteomyelitis.

The wound again healed, but a persistent fistula remained. The patient was discharged on March 6.

She was readmitted on June 2. She continued to lose weight, and was becoming more anemic, emaciated and weakened, the temperature was low grade. Exploration of the sinus at the time traced it down to a large perinephric abscess which contained several ounces of pus. There was still limitation of the right half of the diaphragm. The source of the trouble was finally thought to be located. The wound healed in a few weeks, but again a sinus tract which was discharging seropurulent exudate remained. She was discharged on August 9, and readmitted two weeks later. On her last admission, a roentgenogram still showed limitation in excursion of the right half of the diaphragm with infiltration in the right base. Guinea-pig inoculation of the sputum failed to produce tuberculosis. She continued down hill and her septic appearance became progressively worse. Blood culture was sterile. The sinus continued to discharge.

One morning, November 10, while sitting up in bed she suddenly went into collapse and died, about seventeen months after her first admission.

On postmortem examination, a huge abscess of the liver was found in the right lobe, which had perforated into the subphrenic space. The liver was firmly bound to the wall of the chest by cartilaginous-like adhesions. The diaphragm was also adherent to the liver. The abscess appeared very old, as its wall was unusually thick and cut like cartilage. The right lung showed a considerable degree of fibrosis with dilatation of the bronchioles and bronchi. There were several small abscesses in both lungs.

The abscess was undoubtedly primary and was completely overlooked. The perinephric collection of pus was a secondary gravitation abscess. The only suggestive evidence of the existence of this lesion was a persistent elevation and limitation of the right half of the diaphragm. I failed to appreciate the significance of this sign because of my lack of experience in cases of this type.

CASE 8—L. H., a man aged 29, came to the hospital on Jan. 24, 1923, complaining of pain in the right side of the chest, cough and fever. He became ill six weeks before, when his physician advised him to stay in bed for several days, believing that he had the grip. As he did not improve, he was taken to another hospital, where he remained for two weeks. A roentgen examination of the chest then revealed no gross changes. For the past two weeks, he had had severe pain in the right side of the chest and on the day of admission he discovered a tender area over the right side of the chest. He had had chilly sensations and was considerably weakened since the illness.

Examination revealed the patient to be markedly emaciated, anemic and septic. The right side of the chest was almost flat to percussion up to the angle of the scapula, breath sounds were markedly diminished, subcrepitant rales were present. At the lower postaxillary region of the right side of the chest, there was a large fluctuating area which did not pulsate. The first impression was that an empyema necessitatis existed.

The temperature varied usually between 100 and 103 F with elevation to 105 F, respiration was 25, the white cell count was 28,800 with a differential count of 94 per cent polymorphonuclears and 6 per cent lymphocytes. A roentgenogram of the chest disclosed partial obliteration of the right costophrenic sinus with the presence of fluid, the right half of the diaphragm was higher than normal, suggesting at that time a lesion below the diaphragm which was also slightly limited in excursion. An incision over this fluctuating area disclosed a large abscess cavity leading in a downward direction and apparently extrapleural. The pus emitted a foul odor resembling that of a colon bacillus infection. A culture of the pus revealed a nonhemolytic streptococcus. The course of the illness continued septic, he had repeated chills, perspired profusely and showed a marked weakness, with wide variations in temperature.

A roentgenogram taken eighteen days after this operation still showed a high diaphragm, but less high than before.

A second operation was done four weeks after the first in order to secure better drainage. A portion of the tenth rib was removed. This did not improve the condition.

On Feb 25, 1923, he suddenly complained of severe pain in the right side of the chest, a choking sensation and difficulty in breathing, he coughed incessantly and raised large quantities of foul-smelling pus.

An abscess had apparently perforated into a bronchus. He improved slightly, although he continued a septic course with severe chills, blood cultures were sterile. His condition became progressively worse until his death, which occurred two months after his admission.

Autopsy revealed a huge abscess in the right lobe of the liver which had perforated into the subphrenic space. The right lung showed marked fibroses and was intimately associated with the diaphragm. The bronchioles and bronchi were moderately dilated. A communication between a bronchus and the abscess in the liver could not definitely be demonstrated, although there were sufficient suggestive evidence that such perforation had occurred at some previous time. The entire pleural cavity was obliterated by dense adhesions. There were a few small abscesses in both lungs.

# THE CAUSE OF DEATH FOLLOWING RAPIDLY THE TOTAL LOSS OF PANCREATIC JUICE<sup>\*</sup>

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AND

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In a previous paper,<sup>1</sup> the fatal effect of continued loss of the entire external secretion of the pancreas after intubation of the main pancreatic duct was described. Death occurred in from five to eight days. At that time the cause of death remained unexplained. A few studies of the blood showed dehydration and reduction in the chloride concentration, and unexpectedly an increased alkalinity in the serum, an observation difficult to explain on the basis of extensive loss of such an alkaline secretion as the pancreatic juice. Further examination of the evidence, however, revealed the fact that these observations on the blood were made in dogs that had vomited considerably, a symptom of the gastric irritability almost always present to more or less severe degree in animals thus deprived of pancreatic juice. Vomiting, it was soon noted, was apt to be severe in animals that drank copiously, or in those given fluid by gavage. When they did not drink or when water was withheld, vomiting was practically absent. The observation of the increased alkalinity of the blood in these early experiments was not deemed a sufficient cause for death. As the return of the secretion to the duodenum rapidly restored an animal to health it was supposed that the juice might contain some substance necessary for life.

A decisive answer to these questions has been made possible by a recent study of such intubated animals, care being taken to prevent loss of gastric contents by vomiting. Full details of these experiments have been reported elsewhere.<sup>2</sup> It was found, briefly, that when total loss of pancreatic juice occurred under sterile conditions and in the absence of vomiting the blood shortly before death showed extreme concentration with marked reduction in base bicarbonate and  $p_H$ , i. e. uncompensated acidosis. Such observations are what one might expect from a consideration of the alkaline composition of pancreatic juice.<sup>2</sup> When severe vomiting occurred in addition, the acidosis was less marked.

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1 Elman R. and McCaughan I. M. J. Exper. Med. **45**: 561, 1927.

2 Hartmann A. F. and Elman, R. J. Exper. Med. **50**: 387, 1929.

absent or even replaced by alkalosis due to the superimposed loss of acid gastric juice, thus explaining the early observations

### PROTOCOLS

The following protocol describes the observations in a typical experiment

PROTOCOL 1—Dog 20 was operated on on Dec 19, 1928, and a cannula was placed in the main pancreatic duct to collect the entire secretion of the pancreas as described before<sup>1</sup> Blood was obtained before operation for chemical analysis The first day 260 cc of sterile pancreatic juice was obtained The amounts secreted in the succeeding twenty-four hour periods were as follows 400, 205 320, 365, 440, 320 and 145 cc Each specimen was clear, odorless and sterile as determined by cultures on blood agar as well as by examination of the sediment from centrifugated samples Death occurred on the eighth day after operation with evidences of marked dehydration, asthenia and gastric irritability The vomiting, however, was minimal and the amount of fluid actually lost in this manner did not exceed 200 cc No treatment was given Blood was obtained thirty hours

#### *Changes in the Blood Serum in Dog 20*

	Before Operation	After Six Days of Drainage
Carbon dioxide content, per cent by volume	55.0	23.5
Sodium chloride, milligrams per 100 cc	600	473
Nonprotein nitrogen, milligrams per 100 cc	30	147
Lactic acid, milligrams per 100 cc	18.0	26.5
Total base, milligrams per 100 cc	152	117
Protein per cent	7.0	9.34
pH	7.40	7.33

before death, that is, on the sixth day of drainage The changes, as shown in the accompanying table, were those of uncompensated acidosis

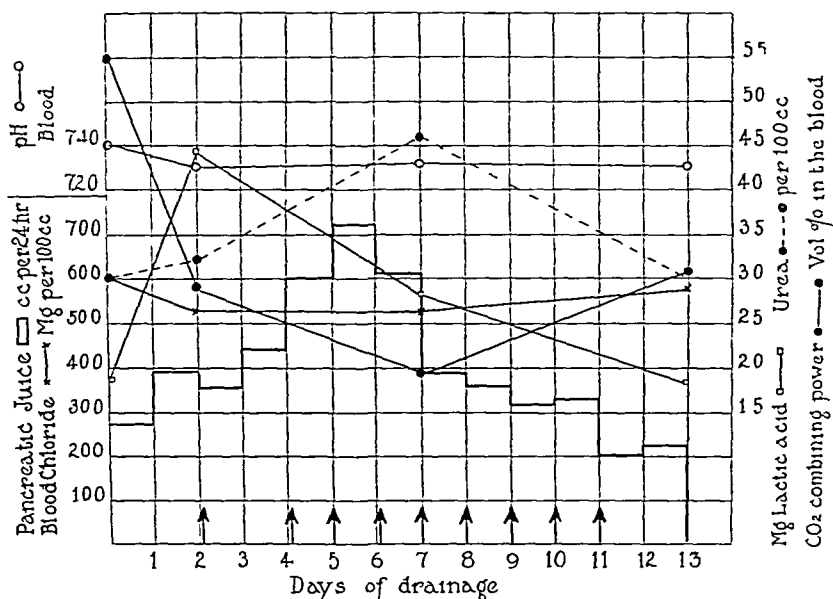
At autopsy, which was performed a few minutes after death, the peritoneum was clear and no infection was noted in the pancreas or collecting system The heart was firmly contracted, the liver was engorged with blood and the blood was so concentrated that it did not flow from the cut aorta or vena cava The stomach was small and contracted, the intestines were empty

It should be emphasized that the method used in these experiments permitted the collection of the entire twenty-four hours' secretion of the pancreas under sterile conditions in a closed system Gamble and McIver<sup>3</sup> recently reported similar observations in two dogs with open pancreatic fistula Their animals lived for several weeks in contrast to the rapid death in our experiments In large measure the difference is probably due to the difference in the amount of secretion lost to the body In dogs draining pancreatic juice through an open wound, the inevitable licking of the fistula restores some of the secretion and the inflammatory changes in the pancreas always present in such cases

<sup>3</sup> Gamble, I. L. and McIver, M. A. J. Exper. Med. 48:849, 1928

often cause a marked diminution in the amount of juice secreted. These circumstances probably account for the longer life in their dogs.

Additional proof that this rapidly fatal outcome was due to simple chemical changes was the fact that death could be prevented and life prolonged during drainage of the pancreatic juice by the administration of sufficient Ringer's solution. When given intraperitoneally or intravenously the response was often marked. The animal became brighter and more active even though continuing to lose large amounts of pancreatic juice. A few dogs have been kept alive with daily injections of 500 cc of solution for weeks and then were killed only because of accidental infection of the pancreatic juice. Though in good general



Observations on dog 23. Each arrow indicates the intraperitoneal administration of 500 cc of Ringer's solution. The animal was killed on the thirteenth day of drainage because of accidental infection of the pancreatic juice.

condition there was always a marked loss of weight. Water alone, or with added dextrose, had no beneficial effects. The following protocol describes one such experiment.

**PROTOCOL 2**—Dog 23 was intubated, as already described, on Dec 29, 1928. The main observations are represented in the accompanying chart. After two days of drainage, the blood had already begun to show the changes mentioned. Ringer's solution was then administered intraperitoneally, 500 cc each day, with marked improvement in the condition of the blood. Special attention was paid to the development of vomiting, which was slight, although the animal showed the usual signs of gastric irritability. Food and water were taken slowly and in small amounts. On two occasions 300 cc of milk was given by gavage. Within a few minutes retching began and soon the entire amount was vomited.



On the thirteenth day of drainage, the dog was killed with chloroform because of accidental infection of the pancreatic juice. As a result the secretion was reduced somewhat in amount, became turbid and was foul in odor. Culture showed *B. coli*. The general condition of the animal remained good. The weight was 8 Kg, a loss of 4 Kg from its preoperative level. At autopsy, the intestines were empty. There was no infection of the peritoneum, and the incision was healed. The stomach was small and contracted. When the duodenum was opened, three deep ulcers were found just distal to the pylorus. The largest one was about 1 cm in diameter and was covered with a dark blood clot which was easily removed revealing a fairly deep base, down to the muscularis.

It is to be noted that the base bicarbonate did not return to the normal level. In more recent experiments a more effective solution containing sodium lactate was used.<sup>2</sup> The results following its use were much more striking, and the return of the blood to normal was more complete.

#### COMMENT

It would seem that death should be prevented or postponed by some mechanism that would diminish the amount of pancreatic juice secreted or lower its concentration of inorganic salts since it is the loss of these salts and water that is really responsible for the fatal result. Yet, in the absence of infection or obstruction, neither of these things take place. The amount secreted remains high even in the absence of any food stimulus,<sup>1</sup> and its base and bicarbonate content stays up to the end, as shown in our experiments<sup>2</sup> by the daily analysis of the pancreatic juice. The pancreas, it would seem, secretes a juice of more or less constant composition even when its constituents in the blood are reduced to a very low level. The same fact has been established for the gastric juice by Lim and Ni.<sup>4</sup> They found that the chloride concentration of the gastric juice, obtained by repeated histamine or psychic stimulations, remained high even when the chloride content of the blood was depressed thereby to a very low level.

Probable reasons why dogs intubated in this way for the collection of total pancreatic juice cannot tolerate food or water by mouth as normally have been mentioned before.<sup>1</sup> From a variety of evidence it was supposed that the removal of the alkalinizing pancreatic secretion<sup>5</sup> prevented neutralization of the gastric contents which, therefore, remained highly acid, could not be tolerated by the duodenum and were vomited. The present observations add support to this supposition. The gastric irritability of dog 23, already described, was marked at all times even though the general condition was good and the composition of the blood was approximately normal. The ulceration noted was found in three dogs, all kept alive for two weeks or longer by means of injections of physiologic solution of sodium chloride. This lesion of

<sup>4</sup> Lim, R. K. S., and Ni, T. G. *Am. J. Physiol.* **75**: 475, 1925.

<sup>5</sup> Elman, Robert. Probable Influence of Pancreatic Juice in the Regulation of Gastric Acidity, *Arch. Surg.* **16**: 1256 (June) 1928.

itself could explain the gastric irritability and vomiting. Of wider interest, however, is the fact that this observation adds support to the theory that high gastric acidity is a factor in the causation of duodenal ulcer. Further observations will be reported later.

Clinically, these observations emphasize the importance of the pancreatic juice in cases involving loss of gastro-intestinal secretions. Such a loss occurs in a variety of conditions, such as prolonged bilious vomiting, intestinal fistulas or obstruction below the pancreatic duct and protracted diarrhea. Loss of pancreatic juice, if sufficient and continued, can of itself bring about a fatal outcome and explains the observation of acidosis in some cases. Loss of gastric juice, of course, also takes place in most cases and indeed is usually the more prominent factor, thus explaining the alkalosis. In either case, however, a marked dehydration occurs, which is probably the most important factor involved. The simple chemical solution containing sodium lactate<sup>2</sup> has actually been used in many such clinical cases with striking results. These will be reported later.

#### SUMMARY

From the observations herein reported, the cause of death following total loss of sterile pancreatic juice seems definite and simple. A profound dehydration results with marked loss of base bicarbonate and resulting uncompensated acidosis. The acidosis may be less marked or may even give way to a slight alkalosis if severe vomiting takes place with the superimposed loss of acid gastric juice. In either case, however, the dehydration with resulting changes in circulation is probably the main factor in the rapid death. That the fatal outcome is due to such simple chemical changes is also shown by the recovery and prolongation of life during drainage of pancreatic juice by the administration of a simple physiologic solution of sodium, potassium and calcium chloride. The clinical application of these observations has been briefly discussed.

# FORTIETH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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(Concluded from p 172)

## MISCELLANEOUS

*Injuries of the Hand*—Bunnell<sup>32</sup> pointed out the common errors which should be avoided in the treatment for injuries of the hand. Incisions should be well chosen and of adequate size. They should not sever the tendon pulleys in the fingers nor cut the nerves in the fingers or palms, especially the motor thenar nerve. The most pernicious incision and unfortunately the one usually made was the median longitudinal one, whether in the palm, wrist, finger, pulp, matrix or dorsum of the finger. It wrecked the hand, caused flexion contractures by being at right angles to the flexion creases, cut the pulleys, caused adhesions at the worst place, namely, the gliding surfaces of the tendons, and was poor for drainage. In the fingers the incisions should be mid-lateral and not anterolateral where they will cut the nerves, in the hand they should follow as much as possible the natural creases. Drains ought not to be left in longer than two days, and large hot compresses of boric solution with 0.5 per cent sodium citrate should be used together with local and bodily rest. Traumatized wounds should not be sutured without debridement. When an incision is made in the

hand, a tourniquet should always be used. Tendons should not be sutured more than twenty-four hours after an injury, as infection is almost inevitable. The exact type of infection present should always be diagnosed before one proceeds with the treatment. Infections of the tendon sheaths or palmar spaces ought never to be treated in an office. Local anesthetics should be avoided unless of the nerve block type. The wrist, hand and fingers ought to be kept in the position of optimum function during healing.

[ED NOTE—Bunnell has had extensive experience with injuries and infections of the hand, and we feel that his advice should be heeded. The article deserves the careful study of surgeons handling this class of work.]

*Dupuytren's Contraction*—Kanavel, Koch and Mason<sup>33</sup> reported the results of their studies of Dupuytren's contraction together with the twenty-nine cases on which it was based. Seven of the patients had been operated on previously, some of them more than once, in spite of which the condition had recurred. The results observed in such patients and the results obtained in the patients operated on by the authors impressed them with the importance of the following: 1. Wide excision, not only of the contracted fascia but of all its attachments to the skin, the interfascial septums, the volar interosseous fascia, the metacarpal bones and the phalanges. In case of doubt they preferred to err on the side of removing apparently normal fascia, and they considered this an added guarantee against recurrence. 2. Careful dissection and elevation of the skin to avoid trauma and subsequent necrosis. 3. Painstaking effort to avoid injury or division of the digital nerves and blood vessels which were frequently embedded in the bands of fibrous tissue which draw the fingers into flexion. 4. Excision of skin that is hopelessly involved and replacement of the excised skin by a free full thickness graft rather than an attempt to bring together the edges of the wound under tension. 5. In long-standing cases with marked contraction of the fingers, excision of the head of the proximal phalanx and shortening of the extensor tendon of the affected fingers through a dorsal incision (Hutchinson's operation). 6. Active movement of the fingers and hand as soon as the operative wound is soundly healed.

The authors were of the opinion that if treated in such a manner complete restoration of function might reasonably be hoped for, although cellular infiltration of the hand and partial anesthesia and stiffness of the fingers were to be expected for a considerable time after the operation.

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<sup>33</sup> Kanavel A. B., Koch S. L. and Mason M. L. Surg. Gynec. Obst. 48: 145 (Feb.) 1929.

*Pathologic Dislocations of the Femur* —LeFort<sup>34</sup> made a study of simple pathologic dislocation of the hip, meaning by this a dislocation that had occurred as the result of disease but without modification in the shape of the bones sufficient of itself to bring about the dislocation. He found that in tuberculous coxitis, dislocation occurred sometimes suddenly in the early course of the disease but more often gradually at a later period. In acute osteomyelitis, dislocation resulted sometimes from a direct suppurative involvement of the joint, more frequently it was the consequence of a para-articular lesion. It also occurred in the course of rheumatic disease and during convalescence from acute general diseases, especially septicemia and pyemia.

Multiple factors contributed to prepare the way for and to bring about the dislocation. The chief factors were prolonged vicious attitude of the limb, softening of the cotyloid ligament, swelling and effusion in the joint, atrophy of the muscles, particularly of the gluteus maximus, contracture of the antagonistic muscles, and the effects of trauma, often of minimal character. Simple dislocation could not occur unless there was a relaxation of the capsule and ligaments and could not be complete unless the ligamentum teres was destroyed. As a general rule, the dislocation was only an accident in the course of a destructive arthritis and whether or not this was reduced, the usual destructive changes occurred later. When the dislocation was not reduced, however, bony changes developed due to the adaptation to the new position, and at a later period it was often difficult to recognize from the appearance of the hip that it had been a pathologic dislocation.

The treatment for a recent dislocation should take into consideration the treatment for the primary disease process first, but at the same time efforts should be made to reduce the dislocation either by traction and manipulation or by open operation. When reduced measures had to be adopted to prevent redislocation, even when reduction had been accomplished, the final result was modified by the evolution of the disease process and normal function was scarcely ever to be expected, but rather ankylosis or marked destruction of the articular surfaces, the functional effects of which were to be reduced to their minimum by proper therapeutic measures. The treatment for a long-standing pathologic dislocation was essentially the same as that of any long-standing dislocation whether congenital or traumatic.

Gill<sup>35</sup> wrote on the treatment for pathologic dislocation, basing his conclusions on the study of forty-four patients, in all of whom operation was performed. The dislocations were due to tuberculosis, pyogenic and pneumococcus infections, infantile paralysis and encephalitis. Sur-

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34 LeFort, R. *Rev. d'orthop.* **15** 514 (Nov.) 1928.

35 Gill, A. B. *South M. J.* **22** 207 (March) 1929.

gical intervention was indicated to secure stability of the hip, relieve pain, correct deformity and to obtain motion if this was consistent with stability and freedom from pain. The author advised against osteotomy of the femur, since in his experience it did not correct the deformity and left either a painful fibrous ankylosis or a great instability. The author preferred to perform either the reconstruction operation or an arthrodesis, the choice depending on a careful appraisal of all the circumstances of the case.

*Bilateral Snapping Hip*—Dickinson<sup>36</sup> considered true snapping hip to be a relatively unusual condition, and stated that bilateral snapping hip was rare. The usual cause was a thickening of either the iliotibial band or the tendon of the gluteus maximus. He said that operations for relief from the condition ought to be performed with the aid of local anesthesia as it was essential to see which band was at fault; the snap usually disappeared under the relaxation of general anesthesia. He considered early mobilization of the hip following the operation essential.

*Fat in Traumatic Effusions of the Knee Joint*—By the use of special methods Kling<sup>37</sup> was able to demonstrate the presence of a considerable quantity of fat in the synovial fluid of six patients with traumatic hemorrhagic effusions of the knee joint. The interjoint fat deposit and the bone-marrow of the epiphysis were considered to be the source of the fat, hence the presence of fat indicated an injury to the interjoint structures (crucial ligaments and semilunar cartilages) alone or combined with fracture of the articular surfaces. The presence of the fat was demonstrated by centrifugalization of the aspirated fluid which caused it to separate in an easily recognizable layer.

*Eburnation of the Tibia*—Froelich<sup>38</sup> observed four patients with eburnation of the tibia and reviewed similar cases that have been reported in the medical literature. His patients were girls ranging in age from 6 to 12 years. The lesion manifested itself clinically by pain, or in some instances only by tenderness to pressure and by an increase in the volume of the bone. Roentgen examination showed a zone of bone condensation at the level of the middle third of the tibia and a decrease in the size of or a total disappearance of the medullary cavity. According to various authors, this disease might appear in the first weeks of life. The bone was opaque on roentgen examination, broke easily and might fracture spontaneously. Putti gave the condition the name eburnating osteitis, Albert-Schoenberg, marble bone and Leri, hyperostosis.

36 Dickinson, A. M. *Am J Surg* 6:97 (Jan) 1929.

37 Kling, D. H. *Am J Surg* 6:71 (Jan) 1929.

38 Froelich. *Rev d'orthop* 16:1 (Jan) 1929.

*Major Frequency of Orthopedic Diseases on the Left Side*—From Spitzzy's large clinic comprising more than 7,000 cases, Aberle-Horstenegg<sup>39</sup> compiled statistics which showed that diseases of an orthopedic nature involved the male sex and the left side of the body with much greater frequency than the female sex and the right side. This was particularly noted in respect to the hip joint, including such lesions as tuberculosis, congenital dislocation, Perthes' disease and morbus coxae senilis.

*Massage as a Therapeutic Agent*—Massage, according to Jarman,<sup>40</sup> exerted its therapeutic action in two ways—mechanical action and reflex action. Mechanically, it stimulated the circulation of blood and lymph, and acted on tissues and organs by tension and pressure. There was no direct proof of its reflex action, but contraction and relaxation of musculature were observed during massage. Massage produced changes in muscular tissue without producing fatigue. Experiments so far indicated that massage was not accompanied by lactic acid and carbon dioxide formation. Massage should never be used in acute inflammatory conditions. It should be carried out only by trained persons at the order of physicians familiar with the patient's local and general condition.

[ED. NOTE—Much remains to be learned of the action of massage. All observers agree that the effect is not wholly to be explained on the basis of mechanical action. Now that progress is being made in the understanding of physiology of the muscle, it is to be hoped that additional facts will be forthcoming to give one a more rational basis for its use. We believe that Jarman's recommendations are sound.]

*Longitudinal Osteotomy*—In discussing methods of performing osteotomy, Haas<sup>41</sup> stated that the chief desideratum was correction of the deformity with a minimum displacement of the fragments. He described a method that he had found useful, in which he performed a series of longitudinal osteotomies through the entire thickness of the cortex, each about from 3 to 4 cm long and about 1 cm apart. This weakened the bone sufficiently to allow it to yield to a bending force applied in any direction. Rotary deformities could also be corrected without disturbing the continuity of the bone. The time required for healing was less than with the usual transverse osteotomy.

*Operative Substitution of the Thumb*—Joyce<sup>42</sup> recorded the present condition of two patients on whom he had substituted a ring finger of the opposite hand for a thumb.

39 Aberle-Horstenegg, W. Ztschr. f. orthop. Chir. **51** 489, 1929.

40 Jarman, M. B. Virginia M. Monthly **55** 731 (Jan.) 1929.

41 Haas, S. L. Longitudinal Osteotomy, J. A. M. A. **92** 1656 (May 18) 1929.

42 Joyce, J. L. Brit. J. Surg. **16** 362 (Jan.) 1929.

In the first patient operated on twelve years ago, the excellent immediate result was marred later by flexion deformity at the new metacarpophalangeal and interphalangeal joints, and these joints were subsequently ankylosed. Since this ankylosing operation, done seven years ago, the man has worked as an upholsterer, and the new thumb feels to the patient as "if it were his old thumb."

The second patient, operated on nine years ago, has developed a similar flexion deformity at the new metacarpophalangeal joint. The new digit is stable and allows half the extent of passive movement possible in the carpometacarpal joint of a normal thumb, the metacarpophalangeal joint of the new thumb (proximal interphalangeal joint of the old finger) has a flexion deformity of 90 degrees, and only a few degrees of passive movement. The interphalangeal joint of the new thumb (distal interphalangeal joint of the old finger) is not deformed and allows a few degrees of passive movement. Joyce said that the aim of the operation—the provision of a fixed sensitive thumb to which the patient could oppose the remaining fingers of the hand—had not been realized in this case, partly owing to the flexion contracture at the metacarpophalangeal joint and partly to an initial error in technic, whereby the finger was transplanted with its transverse plane nearly parallel to that of the palm of his hand instead of at right angles to it.

*Transplantation of the Thumb Nail*—Sheehan<sup>43</sup> succeeded in transferring a part of the nail from one thumb to the other thumb in a boy aged 16, who had had absence of growth of the thumb nail for two years following an injury. The result was excellent in both thumbs. He pointed out that the nail was epithelial in origin, like the epidermis, and that success was usually to be expected with such tissues. There were several technical difficulties in both the operation and the after care, but it was possible to overcome these by attention to small details.

*Trisacral Fusion*—A new operative technic for the combined fusion of both sacro-iliac joints and of the lumbosacral joint at one sitting was described by Chandler.<sup>44</sup> Exposure of all three joints was obtained by a curved incision with convexity upward passing in the transverse plane across the posterior surface of the sacrum. A modification of Hibbs' method of fusion was employed to ankylose the fifth lumbar vertebra to the sacrum while the method adopted for stabilizing the sacro-iliac joints resembled that described by Gaenslen. The operation had been performed in five patients, and the author considered that the immediate results were of such a nature as to warrant the more extensive trial of the procedure.

43 Sheehan J. E. Replacement of Thumb Nail. *J. A. M. A.* 92:1253 (April 13) 1929.

44 Chandler F. A. *Surg. Gynec. Obst.* 48:501 (April) 1929.



The reason for developing the operation of trisacral fusion was the necessity of relieving patients with pain low down in the back and sciatic pain in whom it was impossible to determine whether the pathologic cause was situated in the sacro-iliac or the lumbosacral joints, also the fact that in certain patients not one but two or all three of the sacral joints participated in producing the symptoms

[ED NOTE—While it is undoubtedly true that in some cases pain in the back is due to a combined lesion of both sacro-iliac joints or of the lumbosacral and one sacro-iliac joint, nevertheless, one of the lesions is usually primary and the other secondary. The secondary lesion will usually clear up with the disappearance of the primary lesion. We should endeavor to improve diagnostic methods in order to differentiate the cause of the back pain rather than to rush in and perform a "gun-shot" type of operation devised with the idea of making up by number of shots for lack of proper aim. This is not to say, however, that the operation of trisacral fusion may not prove to be a valuable procedure under certain conditions when tested by further experience. It is difficult to see how injury to the posterior sacral plexus can be avoided.]

*Extra-Articular Fusion of the Hip*—Albee<sup>45</sup> considered that the indications for extra-articular fusion in tuberculous hip disease were (1) constant relapse of the adduction deformity in spite of proper conservative treatment, (2) recurrence of the adduction deformity following correction by osteotomy, (3) marked destruction of the head of the femur and acetabulum, (4) evidence of recurrence of activity of the disease process, and (5) active tuberculous hip disease in an adult even though the amount of destruction of bone was slight.

He considered it advisable for the surgeon to have at his disposal more than one method of extra-articular fusion in order to meet the individual indications. He described three operative methods that he had employed. He preferred the massive bone graft carefully fitted and mortised to "chip grafts" and the transplantation of the trochanter. He reported thirty-one operative cases, details of which were given in eight

After describing the technic of an operation for extra-articular fusion of the hip in tuberculous disease which resembled the method of Hibbs but was described by the author in 1922, Hass<sup>46</sup> stated that in his opinion the operation was indicated only in adults and then only when the patients were in good general condition and the disease process was in a quiescent stage. He did not agree with Hibbs, who advocated the operation in children even below the age of 10 years. He had performed the operation only in four patients.

<sup>45</sup> Albee, F. H. *Ann Surg* **89** 404 (March) 1929.

<sup>46</sup> Hass, J. *Ztschr f orthop Chir* **51** 495 1929.

Schumm<sup>47</sup> employed an operation for fusion of the hip with what he called an iliotrochanteric strut graft, the graft being taken from the femur and placed in such a manner as to bridge the space between the ilium and the trochanter. He had performed the operation in nine patients with uniformly successful results.

[ED NOTE—The editors would like to make a plea for greater accuracy in the use of the term “extra-articular” in relation to fusion operations of the hip. The difference between intra-articular and extra-articular methods is more relative than absolute, and there are few of the so-called extra-articular methods that do not open the joint at least occasionally.]

*Late Results of Resection of the Semilunar Cartilage of the Knee*—Tavernier and Chappoux,<sup>48</sup> who advocated under certain conditions complete resection of the internal meniscus by medial transverse arthrotomy with division and resuture of the internal lateral ligament, reported the end-results in fifteen patients treated by this method. All the patients were football players, and it was found that thirteen had resumed play after an interval varying from two to twelve months with an average of five months. Of these, eleven had perfect knees; one showed a little limitation of motion and another a slight decrease of strength. Two had not returned to football playing, of these one had a perfect knee and one showed slight increase of lateral mobility. Both of these patients, however, had sustained rupture of the anterior crucial ligament.

[ED NOTE—The operation of transverse arthrotomy with division of the internal lateral ligament reported by the authors seems totally lacking in merit and deserves the strongest condemnation. Even if complete excision of the cartilage were required, which is rarely the case, this could be done readily through the combined anterior and posterior incisions described by Henderson.]

*Synovectomy in Chronic Arthritis*—Allison and Coonse<sup>49</sup> examined the patients at the Massachusetts General Hospital on whom synovectomy had been performed. They considered the procedure particularly valuable in the proliferative type of arthritis, twenty-seven of the fifty patients studied had this condition. They advised against synovectomy in pyogenic or gonorrheal arthritis, unless perhaps in the chronic stage. In 95 per cent of the cases pain was almost entirely relieved and the patients retained nearly as much motion as before operation. The authors also advocated the operation of synovectomy in other joints than the knee under proper conditions.

47 Schumm, H. C. Surg. Gynec. Obst. **48** 112 (Jan.) 1929.

48 Tavernier and Chappoux. Presse med. **37** 179 (Feb. 6) 1929.

49 Allison, N. and Coonse, G. K. Synovectomy in Chronic Arthritis. Arch. Surg. **18** 824 (March) 1929.

[ED NOTE—The editors are less optimistic than the authors about the results of synovectomy. They urge the necessity of a careful selection of cases for the operation.]

*Posterior Capsuloplasty in Certain Flexion Contractures of the Knee*—After reviewing the operations of Murphy, Putti, Smith and Silver for correction of deformities of knee flexion, Wilson<sup>50</sup> described the operation of subperiosteal posterior capsuloplasty of the knee together with the postoperative treatment. The operation consisted in exposing the lower end of the femur through a lateral incision in front of the biceps tendon, which was divided by a Z-shaped tenotomy. The iliotibial band was sectioned transversely and the capsule was stripped subperiosteally from the posterior aspects of the femoral condyles, particular emphasis being placed on thorough stripping of the intercondylar notch. It might be necessary to make a second incision on the inner side of the femur to obtain complete stripping mesially. After the capsule was freed, the knee was manipulated into complete extension, care being exercised not to injure the external popliteal nerve. A split plaster cylinder was then applied to be worn one week. Exercises and massage were started in one week, and weight-bearing with a brace was allowed in eight weeks. The operation had been performed twenty-one times in fifteen patients. The flexion contracture was due to chronic arthritis in thirteen patients and of traumatic origin in the remaining two.

*Lengthening of the Leg*—Carrell<sup>51</sup> reviewed the results in twenty-eight patients on whom he had performed the operation of leg lengthening described by Abbott. In twenty-one patients the tibia and fibula were lengthened, in seven the femur. Following the tibial operations, complications occurred in four cases. In one case distraction of the bones was delayed until the tenth day, when sufficient union had occurred to prevent extension. The second complication was caused by placing the upper pin too near the epiphyseal line so that it gave way when pressure was applied. In a third case the fibula was not entirely divided and the external malleolus was dislocated upward. In the fourth case, a severe hemorrhage from the pin holes presumably due to injury of the posterior tibial vein resulted on two occasions when attempts were made to apply extension and the lengthening was abandoned. The author did not consider the operation difficult or unusually shocking, but it was necessary to observe meticulous care both in the technic of the operation and during the long after-care.

*Treatment for Pes Cavus*—In discussing Scherb's technic for the treatment for pes cavus, Pick<sup>52</sup> stated that it consisted in the trans-

50 Wilson, P. D. *J. Bone & Joint Surg.* **11** 40 (Jan.) 1929.

51 Carrell, W. B. *South M. J.* **22** 216 (March) 1929.

52 Pick, H. *Zentralbl. f. Chir.* **56** 1876, 1929.

plantation of the long extensor tendons of the toes into the metatarsals together with forcible manipulation of the foot by means of Schultze's osteoclast or resection of portions of the os calcis, cuboid and scaphoid. The transplantation of the tendons was alone sufficient in feet that were easily correctible without force. The operation had been performed at the Dortmund Orthopaedic Clinic in thirty-eight patients and end-results had been obtained in thirty-four of these. The results were good in all cases, in some excellent. The anterior arch showed considerable improvement and lowering of the longitudinal arch was obtained in all the cases. He advised in the average case transplantation of the tendon of the extensor longus hallucis into the first metatarsal, of the tendons of the long extensors of the second and third toes into the second metatarsal and the tendons of the third and fourth toes into the fourth metatarsal.

*Subastragalar Arthrodesis*—MacAusland<sup>53</sup> described his technic of subastragalar arthrodesis and reported eight cases in which it had been performed. He considered the operation useful in imbalance due to paralysis and in joint fractures or joint disease. He employed a semi-circular incision, beginning on the dorsum of the foot at the astragalo-scaphoid joint curving under the external malleolus and terminating over the Achilles tendon. By forcibly inverting the foot it was possible to dislocate the subastragalar joint and obtain complete exposure. With a hand saw generous portions were removed from the under surface of the astragalus, the superior surface of the os calcis and from the scaphoid and midtarsal regions. This permitted considerable backward displacement of the foot, the most important advantage of the operation.

[ED. NOTE.—The operation of subastragalar arthrodesis as it is usually performed is so simple and gives such satisfactory results that considerable evidence will have to be presented before we shall be convinced that wide dislocation of the joint as advised by the author is of sufficient advantage to counterbalance the additional trauma which it must cause to the soft parts.]

#### FRACTURES

*Fractures from the Operative Point of View*—In discussing the open treatment for fractures Henderson<sup>54</sup> pointed out the dangers of the method when employed improperly. He listed the fractures of the lower extremity most satisfactorily treated by the operative method as follows: (1) fractures of the astragalus with marked displacement; (2)

<sup>53</sup> MacAusland, W. R. Subastragalar Arthrodesis. Arch. Surg. 18: 624 (Feb.) 1929.

<sup>54</sup> Henderson, M. S. Radiology 12: 214 (March) 1929.

Pott's fracture with the internal malleolus broken off at a high level (3) refractory fractures of the ankle, (4) spiral oblique fractures of the lower third of the tibia, (5) fractures of the patella, (6) most fractures of the shaft of the femur in adults, (7) fracture dislocations of the hip, (8) slipped epiphysis of the upper end of the femur in children. Of the injuries of the upper extremity, he considered that the following often required operative intervention: (1) overriding fractures of the metacarpals, (2) badly comminuted fractures of the scaphoid, (3) fractures of both bones of the forearm, (4) most fractures of the lower third of the radius other than Colle's fractures, (5) most fractures of the head of the radius, (6) fractures of the olecranon process, (7) epiphyseal separation at the lower end of the humerus with anterior displacement of the lower fragment, (8) fractures of the surgical neck of the humerus with overriding, (9) fracture dislocations of the head of the humerus.

*Closure of Compound Fractures by Skin Plastic*—Cannaday<sup>55</sup> advocated the closure of compound fracture wounds by skin plastic rather than to leave the wound open with the bone exposed, which under the most favorable circumstances resulted in extensive scar formation at the fracture site. The simplest method was to do débridement, make linear incisions on either side of the fracture and free the skin sufficiently so that the edges could be approximated over the fracture.

[ED. NOTE—We agree with the author as to the advisability of covering exposed bone with skin, provided free drainage can be instituted from the sides.]

*Fractures of the Clavicle*—From a review of the treatment of 422 patients of both sexes, adults and children, with fractured clavicles, Lester<sup>56</sup> concluded that with any type of ambulatory treatment the functional results were uniformly good. He advised a simple comfortable dressing (sling, swathe or binder), rather than intricate apparatus designed to hold the fragments in place.

*Fractures of the Lateral Humeral Epicondyle in Children*—After a review of 160 case records and a study of sixty children between the ages of 4 and 8 years with fractures of the external condyle, Massart and Cabouat<sup>57</sup> separated these injuries into three classes: (A) fractures and epiphyseal separations without displacement, (B) fractures with outward displacement with or without tilting of the fragment, the displacement being limited by the capsuloperiosteal attachments, (C) fractures where the fragment has broken loose from its attachments and gross displacement has taken place.

<sup>55</sup> Cannaday, J. E. *Ann Surg* **89** 579 (April) 1929.

<sup>56</sup> Lester, C. W. *Ann Surg* **89** 600 (April) 1929.

<sup>57</sup> Massart, R. and Cabouat. *Rev. d'orthop* **15** 475 (Nov.) 1928.

In group *A* there were fifty-one cases of subperiosteal fracture or epiphyseal separation without displacement, and all yielded excellent results

In group *B* there were forty cases with outward displacement, but without tilting, and nineteen cases with tilting. Of the latter, thirteen patients obtained perfect results, four showed some deviation of the carrying angle and two had considerable limitation of motion.

In group *C* the results of conservative treatment were poor. The fragment was separated from its ligamentous attachments and deprived of blood supply, resulting in necrosis of the epiphyseal cartilage of the condyle and arrest of growth. This factor was more important in accounting for the poor prognosis than the extent of the displacement. Increasing cubitus valgus developed as a result of the cessation of growth of the outer half of the condylar portion of the humerus, and in time was likely to cause a delayed ulnar palsy. The poor results in this group of fractures would seem to point to the advisability of early operative intervention with replacement and suture of the loose fragment.

*Injuries of the Lower End of the Radius*—Edwards and Clayton<sup>58</sup> examined, two years after injury, the late results of 424 fractures of the lower end of the radius, 339 of which were of the Colles type. In 73 per cent there was no disability, 23 per cent complained of minor aches, but were able to carry out their normal occupations, and of these a third had arthritis of the wrist before the injury. In 4 per cent the results were bad. Persistent tenderness over the internal lateral ligament was common, but usually disappeared under physical therapy. Full rotation was usually regained after the patient had returned to work. Many of those in whom limitation of rotation persisted were cured by a manipulation of the forearm under nitrous oxide anesthesia. The poor results were attributed by the authors to (1) a preexisting arthritis of the wrist joint and (2) failure to reduce the backward tilt of the lower radial fragment.

Grasby and Trick<sup>59</sup> also reviewed the results of fifty Colles' fractures two years after the injury. They concluded that a good result invariably followed a good reduction, and that if displacement persisted the result was almost as invariably unsatisfactory on account of a traumatic arthritis of the radio-ulnar joint. Nonunion of the styloid of the ulna did not affect the functional result.

Thurston Holland<sup>60</sup> drew attention to the fact that a genuine epiphyseal fracture of the lower end of the radius is one in which

58 Edwards H. and Clayton L. B. *Brit. M. J.* **1** 61 (Jan. 12) 1929.

59 Grasby E. D. and Trick S. R. *Brit. M. J.* **1** 391 (March 2) 1929.

60 Holland C. T. *Proc. Roy. Soc. Med.* **22** 23 (March) 1929.

the fracture was exclusively in the line between the cartilage and the diaphysis without any injury to the latter, was rare. In practically every case there was some diaphyseal injury as well, and this was seen in the lateral roentgenograms as a small wedge of bone torn off from the edge of the diaphysis. This enabled a diagnosis of "separated epiphysis" to be made by roentgenography even when the displacement had been reduced.

[ED. NOTE—This also accounts for the fact that arrest of growth following separation of the lower epiphysis of the radius is rare.]

*Fractures of the Transverse Processes*—Hartwell<sup>61</sup> reported the results of a study of twenty patients with isolated fractures of the transverse processes of the lumbar vertebrae. The processes of the third and fourth lumbar vertebrae were involved most frequently. Healing was usually by fibrous union. One third of the patients were discharged from treatment in six weeks, free from pain. The other patients continued to have pain, one for a period of more than three years. Five of the patients were submitted to operation, and the transverse processes were removed. In these the duration of the disability averaged less than six weeks, with complete cure in all cases. He considered the group too small to justify more than tentative conclusions.

[ED. NOTE—We should like to see the report of the results in a larger series of patients before advocating excision of these fractured transverse processes.]

*Compression Fractures of the Spine*—Davis<sup>62</sup> considered that the treatment for compression fractures of the spine should aim at correction of the kyphotic deformity and securing proper alignment just as much as reduction was sought in fractures elsewhere. He had been able to obtain this by actively hyperextending the patient on a Bradford frame or plaster shell, or when the posterior spinal arch was intact, by careful manipulative treatment, forcing the spine into hyperextension followed by the application of anterior and posterior plaster shells. A roll in the form of a life preserver was attached to the posterior shell under the point of the kyphos. The patient was kept in the plaster shell for seven weeks, after which a Taylor back brace was applied to be worn in bed for two weeks followed by gradually increasing weight bearing. He reported cases in which the manipulative method had been successfully used, including four cases of fracture dislocation with involvement of the cord. The entire group on which the report was based comprised twenty-nine patients.

[ED. NOTE—Davis has made an important contribution in advocating an active policy with regard to the correction of bony deformity in spinal fractures. In his hands the manipulative method has yielded

61 Hartwell J. B. *Colorado Med.* **26** 37 (Feb.) 1929.

62 Davis A. G. *J. Bone & Joint Surg.* **11** 133 (Jan.) 1929.

good results, whether or not it is free from dangers will have to be demonstrated by further experience. We shall be interested to compare the results of this method with those obtained by Rogers, who used a method of gradually increasing hyperextension on a special hyperextension frame which is soon to be reported.]

*Kummell's Disease*—Wier<sup>63</sup> encountered eight cases of Kummell's disease the symptoms developing from a few months to a year after a severe injury to the back. He deprecated the too great dependence on a single negative roentgen examination, following which the patient received no treatment until spinal deformity and the typical nerve root symptoms developed. In the way of treatment, he advised fixation of the hyperextended spine in a plaster jacket applied in such a way that the weight of the shoulders was borne on the pelvis and the load removed from the vertebrae.

*Fractures of the Shaft of the Femur*—Campbell<sup>64</sup> treated patients with fractures of the shaft of the femur by manual reduction followed by immobilization in a plaster of paris spica casing, and after a large experience believes that it was the most reliable method of treatment. He employed an orthopedic fracture table equipped with apparatus for roentgen examination. Under full anesthesia the fragments were reduced by traction and angulation the ends being made to impinge and interlock, and the position controlled by immediate roentgen examination. A double plaster spica was then applied with the hip and knee flexed.

He deprecated repeated manipulations. The most difficult type of fracture to treat was the oblique, with fairly smooth bone ends. The prolonged immobilization did not cause permanent limitation of motion of the knee. He tabulated the end-results in a group of seventy-one patients whom he had treated, and considered them as satisfactory as those obtained after any other method of treatment. In nineteen patients there was a shortening of  $\frac{1}{2}$  inch (1.27 cm) or more, and in five, of 1 inch (2.5 cm) or more. In only five of the cases was a second manipulation necessary.

[ED. NOTE.—There are several ways of treating almost any fracture, but it does not follow that every one can duplicate the results of some one else, a certain method being used. Campbell is able to obtain good results with fractures of the femur by the manipulative method, but we doubt if this is as safe or reliable a method in the hands of the average surgeon as the traction method of treatment. It must be particularly difficult to hold the comminuted and oblique fractures in proper alignment in a plaster casing.]

63 Wier, S. T. *Texas State J. Med.* **24**: 699 (Feb.) 1929.

64 Campbell, W. C. *Radiology* **12**: 106 (Feb.) 1929.



*Fractures of the Lateral Tuberosity of the Tibia*—Cubbins, Conley and Seiffert<sup>65</sup> called attention to the increasing frequency of fractures of the lateral tuberosity of the tibia which they thought might well be designated "bumper" fractures owing to the fact that they so commonly resulted from collision with an automobile bumper. Forcible abduction of the tibia on the femur was the common mechanism. Improper treatment resulted in a loose joint with genu valgum and permanent disability. If the tuberosity was widely separated, it might be reduced manually or with the aid of a mallet. If the fragments could not be replaced, an open operation should be performed. They had found by arthrotomy that in some of these cases the lateral meniscus was torn loose and its outer rim was displaced down between the fragments, where it prevented reduction. The authors considered it a mistake to remove the meniscus, as its broad cartilaginous surface would surely help to render the joint more stable in case of resulting irregularity of the upper joint surface of the tibia. Replacement of the cartilage was the better treatment.

*Astragalectomy for Fracture of the Astragalus*—Graham and Faulkner<sup>66</sup> advocated astragalectomy in fractures involving the body of the astragalus with displacement when it was impossible to reduce the fragments. They believed that a stable painless ankle with from 20 to 25 degrees of motion could be obtained by the operation, and that this was to be preferred to the stiff and painful ankle which commonly resulted without astragalectomy. They had followed up ten patients on whom astragalectomy had been performed. Of these, eight had severe fractures of the body of the astragalus, and only three were seen for the first time within one month of the injury, the rest being late cases. Five of the ten patients had painless, stable feet, and had returned to their former occupations, two had fair results, and three had definitely poor results.

#### DISLOCATIONS

*Anterior Dislocation of the Elbow*—Anterior dislocation of the elbow, according to Tees and McKim,<sup>67</sup> was a rare type of injury, only thirty-one cases having been reported in the literature, and only twenty-three of these being true anterior dislocations of both bones. They had seen two patients with this condition, both being children. In one, the injury followed a blow on the flexed elbow, in the other, the forearm was caught and pulled in the belt of a cement mixer. Both dislocations were reduced by manipulation without difficulty, and the recovery was complete in both cases.

65 Cubbins W R, Conley, A H, and Seiffert, G S. *Surg Gynec Obst* 48 106 (Jan) 1929.

66 Graham W T and Faulkner D M. *Ann Surg* 89 435 (March) 1929.

67 Tees, F J and McKim L H. *Canad M A J* 20 36 (Jan) 1929.

*Costovertebral Luxation*—Stewart and Warren<sup>68</sup> were able to find records of only ten cases of costovertebral luxation in the literature. They had treated a patient in whom the first rib was dislocated downward following a severe injury. Anesthesia was present around the inner condyle of the humerus and along the ulnar surface of the forearm and over the ring and the little finger. The dislocation was reduced by operation which showed the head of the rib displacing the lower portion of the brachial plexus. The sensory disturbance disappeared immediately after operation.

#### RESEARCH WORK

*Viability of Transplanted Bone*—Pollock, McKenney and Blaisdell<sup>69</sup> transplanted bone with periosteum into the knee joint, abdominal cavity and muscles of dogs and studied the effect on the transplant. Two inch (5 cm.) pieces of rib fractured transversely were used as transplants. Some were transplanted as such, others were enclosed in collodion membranes. In the latter, death of the transplant invariably occurred because the membrane prevented ingrowth of new blood vessels. New bone formation occurred only when the transplant itself became well surrounded by fibrous tissue well supplied with blood vessels. The transplants seemed to survive best when transplanted in muscle. New bone formation in the abdominal cavity took place in only one instance while all the transplants into the knee joint died.

*Effect of Bone Transplantation on the Blood Calcium Level*—Halperin and Walsh<sup>70</sup> attempted to duplicate the work of Schmidt and Obiastzow of Leningrad, who stated that they were able to raise the blood calcium level by homogeneous and heterogenous bone grafts. The Russians transplanted the graft to the pectoral region between the skin and fascia in six persons. In those with the homogeneous graft there was a 9 per cent rise in the blood calcium, while in those with the heterogenous graft there was a 4 per cent raise. They believed that the graft acted not only as a depot of calcium but also as a foreign body in response to which calcium ions were absorbed into the circulation.

Halperin and Walsh, however, experimenting with rabbits and dogs were unable to reproduce these results. They used three normal dogs and three normal rabbits, and made weekly observations on the blood calcium for four weeks. They found no appreciable changes and con-

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68 Stewart S. F. and Warren J. W. Luxation of the Costovertebral Joints, *J. A. M. A.* **92** 605 (Feb. 23) 1929.

69 Pollock W. E., McKenney P. W. and Blaisdell F. E. Viability of Transplanted Bone. *Experimental Study*, *Arch. Surg.* **18** 607 (Feb.) 1929.

70 Halperin G. and Walsh E. L. The Effect of Bone Transplantation on the Blood Calcium Level. *Arch. Surg.* **18** 819 (March) 1929.

cluded that the changes observed by Schmidt and Obrastzow were within normal limits

They admitted however, that their animals were not in a state of hypocalcemia and that possibly a bone transplant might elevate the calcium level in such a condition

*Effect of the Thymus on the Consolidation of Fractures*—Glassner and Hass<sup>71</sup> studied the healing of fractures and the influence on the rapidity of healing of thymic extract. Employing cats for their experiments, they extirpated the thymus and produced fractures of uniform type. One half of the animals operated on was given daily injections of thymic extract for a period of fourteen days, while the other half was used as a control. The progress of healing was followed by roentgen examination every eight days, and at the end of four weeks the animals were killed and the specimens of bone were obtained. The animals that had not received thymic extract showed a much more feeble callous than normal, while the animals that had received thymic extract showed complete consolidation. In a second series of experiments they compared the effect of other glandular extracts with that of the thymus, but the latter always exhibited the greatest effect in hastening the healing of the fracture.

*Importance of Vessels in the Round Ligament to the Head of the Femur*—Zemansky and Lippmann,<sup>72</sup> in a series of rabbits 2 weeks old, sectioned the ligamentum teres on one side, thereby obliterating the circulation through it to the femoral head in order to determine the effect of this procedure on the developing capital nucleus. The specimens were examined from six to thirty-six days later. The changes observed in the femoral heads were anemia, necrosis, signs of cessation of ossification in this area, gross deformation of the femoral head and coxa vara.

They concluded that the vessels of the round ligament were essential, at least in rabbits, for the normal development of the femoral head. Furthermore, as adolescence progressed, the importance of these vessels gradually diminished, until the epiphysis united with the shaft, at which time in normal animals the nutrition was derived entirely from below. They thought it reasonable to suppose that similar conditions prevailed in human beings at the same relative period, i e, the period during which coxa plana or osteochondritis juvenalis appeared. If this supposition was correct, it was not unlikely that the cause of the disease was to be found in some maladjustment of the delicate physiologic balance that existed between these sources of nutrition to the femoral head.

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71 Glassner, K. and Hass, J. *Presse med* 37 176 (Feb 6) 1928

72 Zemansky, A. P., Jr., and Lippmann, R. K. *Surg Gynec Obst* 48 461 (April) 1929

## THE RESORPTION OF BONE

A CONSIDERATION OF THE UNDERLYING PROCESSES PARTICULARLY  
IN PATHOLOGIC CONDITIONS \*

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The earliest workers in bone were concerned with its resorption. Howship,<sup>1</sup> in 1815 and 1817 discussed physiologic and pathologic resorption but others before him had already called attention to this subject. Later Koelliker,<sup>2</sup> using the newer methods of histologic technique, applied himself especially to a study of physiologic resorption and recognized the importance in this process of the multinucleated giant cell which he called osteoclast (bone breaker). Many of his conclusions in regard to the osteoclast have been applied in their entirety to pathologic resorption, with the consequent neglect of other factors which play a part in such resorption. Even physiologic resorption is not brought about solely by osteoclasts.

Physiologic resorption was recognized many decades ago as important in the development of the skeleton which is reconstructed several times before it reaches its adult form. Physiologic resorption can be studied when the cartilaginous skeleton is removed and replaced by the coarse-fibered bone of the primary skeleton. Later the primary bone is resorbed and replaced by lamellar bone.<sup>3</sup> That constant physiologic resorption goes on in lamellar bone was recognized long ago, but the physiologic and chemical importance of this reconstruction has recently been brought into relief, as it has been bound up with the subject of mineral metabolism.

In this paper, I shall deal chiefly with the subject of pathologic resorption. It is sometimes difficult to draw the line between physiologic

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1. Howship, J. Experiments and Observations in Order to Ascertain the Means Employed by the Animal Economy in the Formation of Bone. *Med.-Chir. Tr.* 6: 263, 1815. Observations on the Morbid Structure of Bones and Attempt at an Arrangement of Their Diseases. *ibid.* 8: 57, 1817.

2. Koelliker, A. Die normale Resorption des Knochengewebes. Leipzig: F. C. W. Vogel, 1873.

3. Jaffe, H. L. The Structure of Bone with Particular Reference to Its Fibrillar Nature and the Relation of Function to Internal Architecture. *Arch. Surg.* 19: 24 (July) 1929.

and pathologic resorption. For instance, should old age osteoporosis and inactivity osteoporosis be classed under physiologic or pathologic resorption? In a discussion of resorption of bone in general, such as this is, it is not necessary to make such distinctions. The resorption varies with the individual conditions that are producing it, but I do not plan to discuss in detail how these resorptive processes vary in specific diseases. Pathologic resorption is seen in acute and chronic inflammatory diseases of bone, it occurs in all localized resorptive processes in connection with tumors and aneurysms, in metabolic bone disease resorption is often prominent, in the reconstruction of callus and transplants and in the dissolution of callus and sequestrums various degrees of resorption are seen.

I shall aim to give a balanced conception of pathologic resorption. A survey of the literature shows that previous discussions have frequently been limited to one phase of the problem, resulting in its over-emphasis. The conclusions drawn concerning the pathogenesis of pathologic resorption must be interpreted with regard to the material used in the investigation. The development of resorption brought about by the ingestion of acids or acid salts will differ in several ways from that due to starvation, and the process of resorption in these two will be different from the resorption of bone in acute inflammatory diseases. In addition to the basic etiologic factor, the resorptive picture is influenced by the severity and acuteness of the process.

Resorption may be accomplished by osteoclasts or by blood vessels and granulation tissue. There has been much controversy as to whether or not a preliminary decalcification of the bone is necessary before there can be resorption by osteoclasts and blood vessels. The importance attached to the part which the lacunae and canaliculi of the bone cells play in resorption has varied considerably. There has been a tendency to attach too much importance to the resorption of bone by osteoclasts. Osteoclastic resorption plays rather an insignificant part in the more fulminating inflammatory bone diseases.

Vascular resorption, mentioned in 1793 by Weidmann<sup>4</sup> and in 1817 by Howship, was first described as a widening of the existing vessel canals. Attention was again focused on it when descriptions of newly formed vascular spaces in resorbing bone were published by Tomes and de Morgan<sup>5</sup> in 1853, and subsequently independently described by Volkmann<sup>6</sup> in 1863. These newly formed vessel canals of bone are now known as Volkmann's canals. The increased vascularization of

4 Weidmann, J. P. Ueber den Brand der Knochen, Frankfurt, A. W. Andreas, 1793, German translation, Leipzig, 1797.

5 Tomes, J., and de Morgan, C. Observations on the Structure and Development of Bone, Phil. Tr., Lond. 143, 109, 1853.

6 Volkmann, R. Zur Histologie der Caries und Ostitis, Arch. f. klin. Chir. 4, 436, 1863.

the marrow, the enlargement of the existing vessel canals and the perforation of both the compact and the spongy bone by newly formed vessels, extending out from the preexisting vessels, rapidly reduce the amount of bony tissue

Howship, in discussing vascular resorption, described the enlargement of the haversian canals, the surfaces of which either remained smooth or exhibited a rough and uneven appearance. The uneven irregular depressions in the walls of the haversian canals, to which Howship called attention, are now known as Howship's lacunae, the name having been extended to apply to all depressions produced beneath the periosteum or endosteum, on the walls of the canals, or on the surfaces of the spongy trabeculae during the course of the resorption of bone.

Following Virchow,<sup>7</sup> who attached much significance to the degeneration of the bone cell and its surrounding bone (cell territories) in resorption and in the formation of Howship's lacunae, were many who advocated his theory and who even modified it to account for the origin of Volkmann's canals from enlarged lacunae and canaliculi of bone cells. These views were assailed by those who ascribed to the osteoclasts the sole and exclusive ability to form Howship's lacunae, and by those who viewed Volkmann's canals as newly formed vessel canals of bone. But there may be some truth in what Virchow and his followers described particularly in regard to the formation of lacunae by local bone cell and matrix degeneration. Vascular resorption can also produce such lacunae in bone.

When pathologic resorption occurs, I believe that the histologic picture is a composite one, owing to the superposition of the pictures produced by the various cellular, vascular and chemical influences exerted on the bone. The resorptive picture in each case is determined by the stimulus to resorption and other factors, such as the particular bone in which resorption is taking place, the age of the subject and the state of nutrition.

This paper is based on a study of the literature of resorption in general, as well as on experience with a large amount of material from this laboratory, illustrating the resorptive processes in bone. The material includes embryonal bones, bone transplants, experimental osteoporosis, acute and chronic inflammatory diseases and bone tumors. The material was studied in a variety of ways. The sections were decalcified in Muller's solution, Muller plus 5 per cent glacial acetic acid, 5 per cent nitric acid or von Ebner's solution. Frozen or paraffin sections were cut and some ground disks were made by the file method using bone fixed in formaldehyde. The sections were studied either unstained or stained by the following methods: Mallory's eosin and

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<sup>7</sup> Virchow, R. *Die Cellularpathologie*. Berlin: A. Hirschwald, 1871, vol. 1.

methylen blue (methylthionine chloride, U S P ) hematoxylin and eosin, Mallory's connective tissue stain, or Foot's modification of the Bielschowsky-Mariesch silver impregnation technic. Most of the methods used have been described in another paper.<sup>8</sup>

#### VASCULAR RESORPTION

By vascular resorption is meant the disappearance of bone through the agency of blood vessels and granulation tissue, resulting in enlargement of the existing vessel canals, the appearance of newly formed vessel canals and changes in the marrow.

*The Vessel Canals of Normal Bone*—To understand vascular resorption a conception of the extent and ramification of the normal vascular channels, both in the bone and in the marrow, is necessary. If a tubular bone is examined, it will be noted that blood vessels are carried through the compact bone by a series of vessel canals which anastomose and communicate with each other, and which convey the blood from the periosteum to the marrow cavity. The surfaces of the spongy trabeculae are for the most part nourished by the vessels of the marrow, but some of the larger spongy trabeculae may contain vessel canals. In adult bone cortex, the system of canals consists of the haversian canals, which run for the most part longitudinally, and the canals of the ground lamellae which run either circumferentially in the ground lamellae or transversely through them. A system of communicating canals connects the haversian canals with each other and like the haversian canals and the canals of the ground lamellae was formed by the deposition of bone around preformed vessels. A typical haversian canal usually contains at least two capillary vessels and some connective tissue. The larger ones may contain fat and lymphoid marrow.

The vessel canals of the cortex, as seen in a longitudinal section, appear as a continuous anastomosing and ramifying network beneath the articular cartilage at the upper or lower end of a bone, a longitudinal section discloses a number of haversian canals in cross-section, which means that in this region the haversian canals have changed their direction and run transversely to the long diameter of the bone. Some of the larger spongy trabeculae contain haversian canals that run transversely to the long axis of the bone. The canals of the spongy trabeculae connect with the marrow spaces by means of short, narrow communicating canals which are cut through their long axes in a longitudinal section of the bone.

The canals of the external ground lamellae are a means of connecting the vessels in the haversian canals with the periosteal vessels, and

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<sup>8</sup> Taft, H. L. Methods for the Histologic Study of Normal and Diseased Bone. Arch. Path. 8: 817 (Nov.) 1929.

the vessels in the haversian canals are connected with the marrow cavity by means of the vessels in the canals of the internal ground lamellae (figs 1 2 and 3) In another paper, I described in detail the vessel canals of normal and pathologic bone<sup>9</sup>

*Changes in the Vessel Canals During Resorption*—In resorption of bone, particularly in the more fulminating and inflammatory diseases enlargement of all the existing canals is well demonstrated in the cortex and a dilatation and increase in the number of blood vessels contained within them The vascular dilatation is similar to the dilatation of

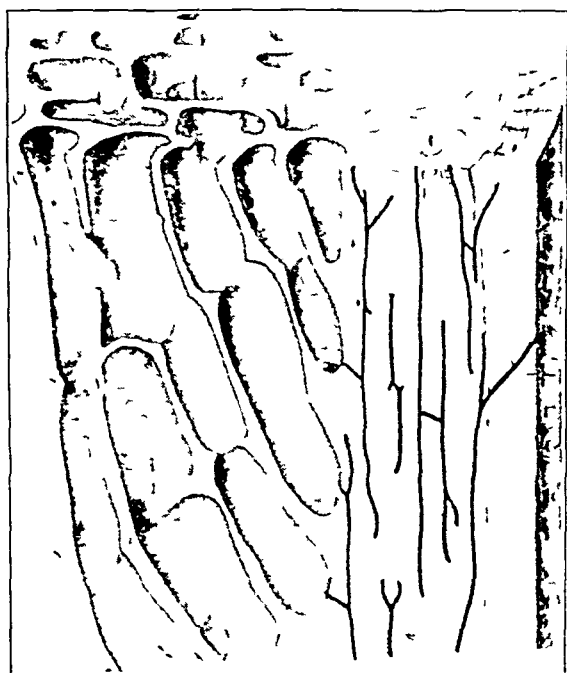


Fig 1—Diagrammatic representation of a longitudinal view of a bone, showing both compacta and spongiosa The cortex on the right shows the outer ground lamellae, with some Sharpey fibers penetrating them The haversian systems are illustrated, and the longitudinally directed haversian canals connected by the communicating canals are shown after Braus

smaller blood vessels everywhere in the body in the course of inflammation and the increased number of vessels results from the proliferation of the vessels already present Concomitantly with this increased vascularization an enlargement of the caliber of the vessel canals occurs If the diaphyseal portion of the compacta from a case of progressive chronic osteomyelitis is examined in cross-section it is found to contain

<sup>9</sup> Iaffe H L The Vessel Canals in Normal and Pathological Bone Am J Path 5 323 1929



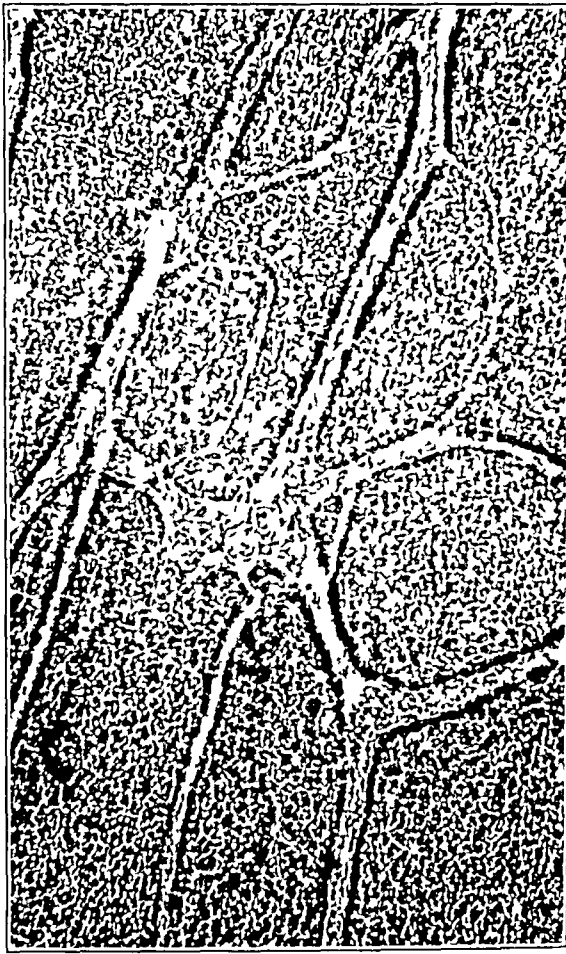


Fig 2—Longitudinal section of normal cortical bone, showing the anastomosing and branching haversian canals. The communicating canals between the haversian canals are demonstrated. The regularity and smoothness of the walls and the narrow lumina of the canals are to be noted. Unstained ground disk,  $\times 75$

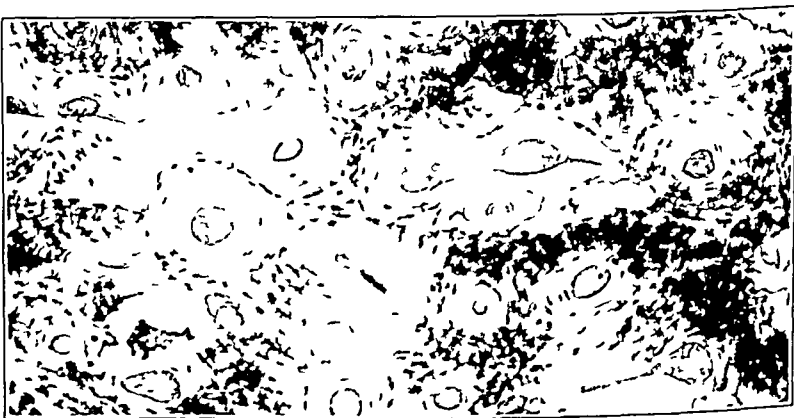


Fig 3—Part of a cross-section of the normal cortex, showing the haversian canals, and in the upper portion of the picture an haversian canal anastomosing with two adjacent haversian canals by means of communicating canals. Note the small diameters of the canals. Unstained ground disk,  $\times 75$

haversian canals, the diameters of which are increased from one to several times. All haversian canals are not uniformly enlarged. Depending more or less directly on the severity of the process, few or many might not be enlarged at all. In cross-section it will also be seen, and this is more common in the severer inflammatory processes, that there is an actual coalescence or tendency to coalesce of several of the enlarged haversian canals, the thin bony partitions between them disappearing completely and resulting in the formation of large spaces in the bone, containing numerous blood vessels and considerable vascular granulation tissue. The enlargement of the canals is not limited to the haversian

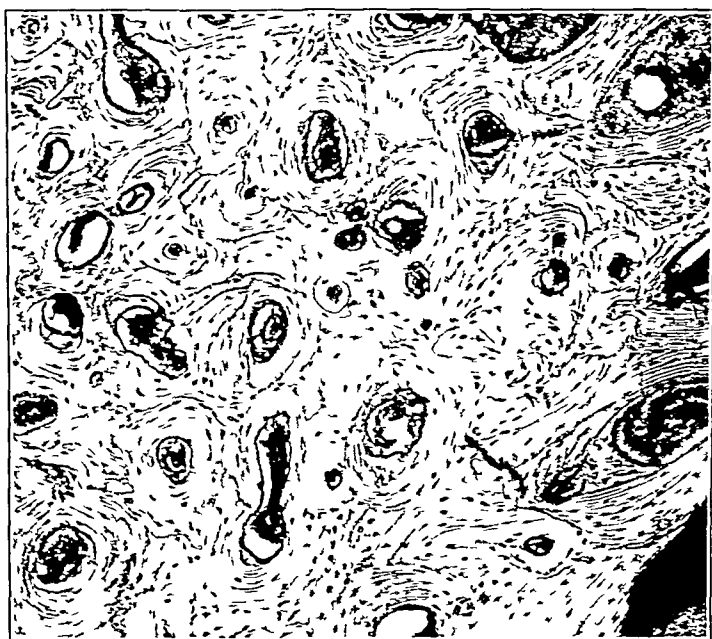


Fig 4—Cross-section of the compacta from a case of chronic osteomyelitis. Many of the haversian canals are much enlarged and filled with granulation tissue. The walls are smooth. An enlarged communicating canal is seen. Frozen section stained with gallium,  $\times 75$ . Compare with figure 3.

canals, but all the canals of the cortex are subject to the same process of enlargement, this being true also of the few canals of the spongy trabeculae (figs 4 and 5).

The enlargement of the existing canals may be in the nature of a uniform enlargement of their caliber, the walls of the canals remaining smooth, or it may be associated with the appearance of indentations on the walls of the canal at various levels. These indentations correspond to those frequently seen on the surfaces of the spongy trabeculae, and are known as Howship's lacunae (fig 6). Such lacunae are not so frequent on the walls of the vessel canals as they are on the spongy

trabeculae, and this is probably due to the fact that the spongy trabeculae are more exposed to granulation tissue in inflammatory processes.

The extent and the course of the canals are also changed during vascular resorption. While the haversian canals usually run longitudinally, in inflamed bone their course becomes tortuous and is lengthened. A longitudinal section of inflamed compact bone will show cross-sections of haversian canals, owing to the fact that these canals, because of their tortuosity, have been cut through a turn in the canal.

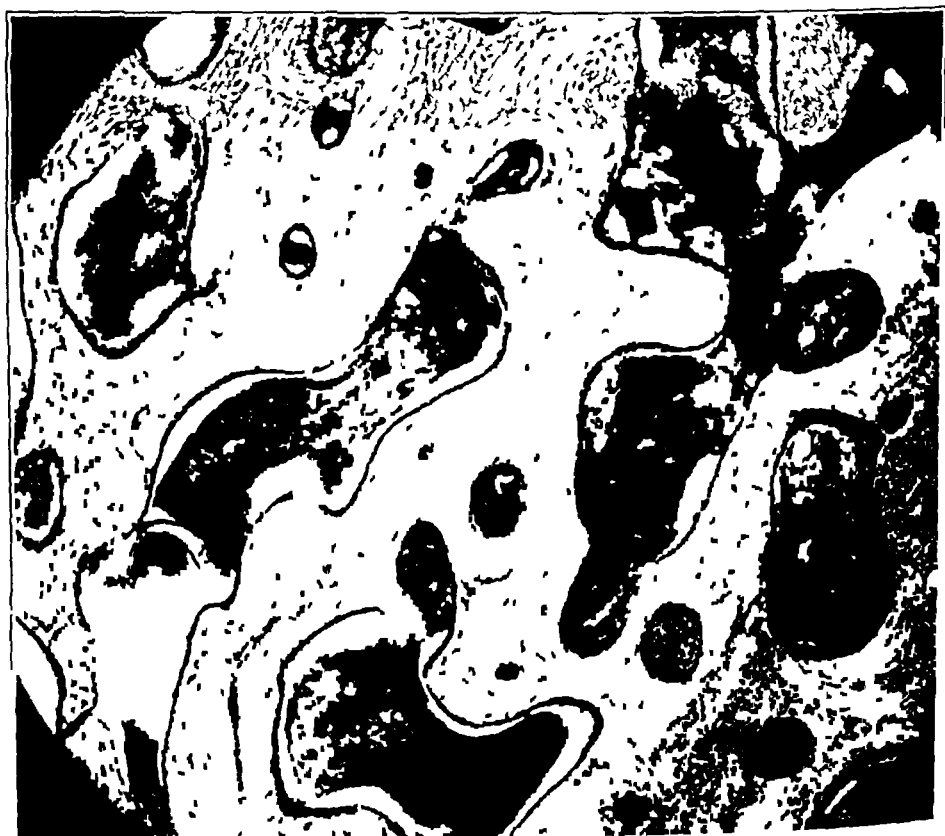


Fig. 5—Cross-section of the compacta from a case of chronic osteomyelitis, showing the spaces formed by the coalescence of extremely enlarged haversian canals. A few haversian canals are still not enlarged. The sinus-like spaces are filled with vessels and granulation tissue. The walls of the spaces are smooth. The spaces extend irregularly through the compacta. Frozen section stained with gilliem,  $\times 75$ .

*New Canals in Resorbing Bone*—Volkmann, in 1863, described the appearance of numerous newly formed vessel canals in the cortex of diseased bone, which differed from the existing canals in size, arrangement and vessel content. These canals had irregular toothed borders and were narrow but of varying caliber. They were not surrounded by concentric lamellae but broke through the lamellae surrounding the

existing blood vessels. Their course was irregular, and sometimes they extended snake-like through the entire thickness of the cortex. These canals have come to be known as Volkmann's canals. In its earliest form, a Volkmann canal appears as a short, irregular, fine crack in the ground substance, radiating from a haversian canal, from which several of them may be seen coming off. As the canal grows, a branch or



Fig 6—Longitudinal section of the cortex from a case of osteomyelitis. The haversian canals are enlarged in diameter, and the walls are irregularly indented showing Howship's lacunae. Compare with figure 2. Frozen section stained with Bielschowsky's silver stain.  $\times 75$

branches from the haversian vessel vascularize it. In vascular resorption of bone the enlargement of the existing vessel canals is more important in reducing the bone substance than the formation of Volkmann's canals (figs 7, 8, 9 and 10).

*Changes in the Marrow During Vascular Resorption*—While these changes are taking place in the cortex the character of the marrow is

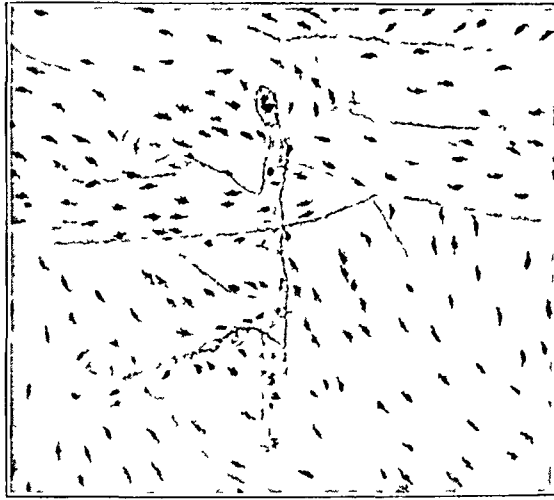


Fig 7—Camera lucida drawing showing the development of three newly formed passages. The larger, vertical one extends from a haversian canal above to one below. Below a fine triangular passage is seen extending through the interstitial and haversian lamellae as it approaches an haversian canal. Some of the characteristics of Volkmann canals are shown. Magnification about 100.

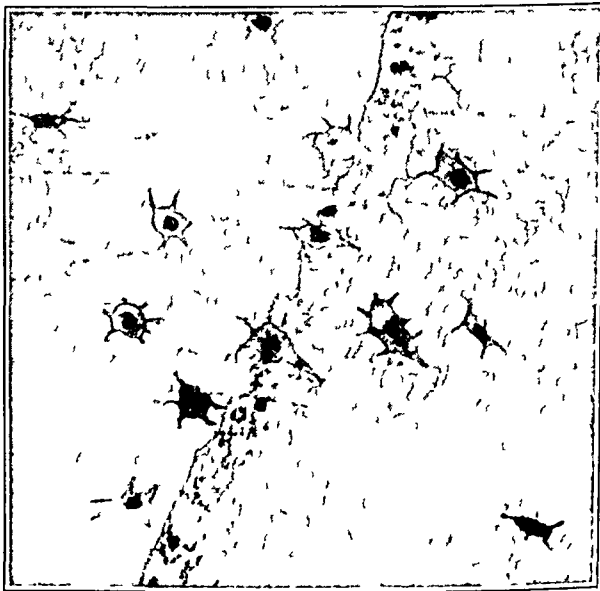


Fig 8—High power camera lucida drawing, showing the details of a crack in the ground substance that will become a Volkmann canal. The crack breaks through the lamellae, including the cement lines, passing directly through the bone cell lacunae that lie in its path. Coarse granules of decalcified material are contained within the crack, along with some nuclear debris. Note the irregular walls of the crack. Magnification about 600.

also altered. Normally the vessels of the marrow are derived from the nutrient artery, which enters the diaphysis through the nutrient canal and from the numerous metaphyseal and epiphyseal vessels which enter the medullary cavity through the thin cortex in the respective regions. The general pattern of the arterial vascular system of bone-marrow has long been known. It is made up of the nutrient artery which divides on entering the marrow cavity, and which gives off one branch



Fig. 9—Section of bone cortex, showing some enlarged Haversian canals and numerous newly formed Volkmann canals criss-crossing through the ground substance. Frozen section, stained with gallien,  $\times 75$

which passes to each epiphysis. These main branches give off finer branches. In the region of the metaphysis and epiphysis numerous nourishing vessels penetrate the cortex of the bone to enter the marrow cavity. While the compact bone receives nearly all its vessels from the periosteum, the nutrient, metaphyseal and epiphyseal vessels on passing through the compact bone also supply some branches to the bone cortex. These branches anastomose within the cortex with vessels that entered from the periosteum. The vessels of the cortex nearest

the medullary cavity anastomose with the marrow vessels. There is, therefore, an extensive anastomotic connection within the cortex between the vessels of the periosteum, and the epiphyseal, metaphyseal and nutrient artery branches, while within the medullary cavity branches of the latter three vessels anastomose with those of the periosteum that have entered after passing through the cortex.



Fig. 10—Cross-section of human adult cortical bone from a case of osteomyelitis, showing enlarged Haversian canals, giving rise to several transverse newly formed, perforating canals of Volkmann. Some of the Volkmann canals join other Haversian canals.

Because of this intimate anastomotic connection, changes that affect the cortex also leave their mark on the marrow. In a severe inflammatory process, the marrow becomes extremely vascularized, as a result of the proliferation of the existing vessels. The newly formed vessels appear as dilated congested channels. Connective tissue also increases,

the lymphoid marrow disappears and is replaced by polymorphonuclear leukocytes with a sprinkling of inflammatory exudative cells in the severer lesions. In the less severe lesions more fibroblastic proliferation is present and greater numbers of lymphocytes, plasma cells, eosinophils and inflammatory exudative cells appear. As a result, there is encroachment of vessels and granulation tissue on the marrow surface of the cortex and on the surfaces of spongy trabeculae which become thinner and smaller and which may appear gouged out owing to the development of numerous depressions which are the Howship's lacunae (fig 11). The speed of the destruction of the spongy trabeculae is dependent on



Fig 11—Section through the rib of a dog suffering from experimental osteoporosis due to calcium deficiency. It shows the atrophic spongy trabeculae, disappearance of the lymphoid marrow which is replaced by a loose connective tissue containing numerous blood vessels, many of which are in apposition with the atrophic spongy trabeculae. Paraffin section stained by Bielschowsky-Marsch silver stain  $\times 75$ .

the severity of the lesion. In the severer lesions the spongy trabeculae seem to be resorbed without osteoclasts. The resorption of the spongy trabeculae must be viewed as analogous to the enlargement of the vessel canals of the cortex. Because of the thinness of the trabeculae and the greater vascularity of the surrounding tissue they are more vulnerable to resorption.

The spongy trabeculae may also be penetrated by newly formed vessel canals and those canals already present may become enlarged.



similarly to those in the cortex. During resorption, the osteoblasts lining the trabeculae and the various canals disappear, and new bone formation ceases. The osteoblasts do not reappear until degeneration takes place. Sometimes in the same section certain areas show resorption still in progress and an adjacent area may show cessation of resorption or the resumption of degeneration. The same trabecula may show resorption on one surface and bone regeneration on the other.

*The Mechanism of Vascular Resorption*—In discussing vascular resorption, I described the changes as they occur when the resorption is acute and extensive. I indicated that the vascular changes in resorption vary with the severity and the cause of the resorption. While vascular factors are associated with the resorption of bone during old age, the changes are not so radical as they are in even a mild inflammatory process, but they are present. There are differences in the character of the vascular changes of resorption in the various inflammatory diseases of bone, which is also true in regard to the resorption caused by varying degrees of calcium deficiency in the diet. The amount of dilatation of the vessel canals depends more or less on the degree of vascularization, the speed and extent of the resorption being less when fewer vessels are present and when the granulation tissue is more cellular.

The question as to how vascular resorption occurs arises. There is no doubt that osteoclasts play little or no part here. In fact, they are rather infrequently seen on the walls of the vessel canals in the more acute resorptive conditions and they seldom appear on the trabeculae in such conditions.

Whether enlargement of the vessel canals and the formation of Volkmann's canals are preceded by a decalcification of the bone has not been decided. It is difficult to conceive that the extensive enlargement of the existing vessel canals and the formation of new vessel canals, taking place at the rate they do under many conditions, should not be preceded by or simultaneously associated with decalcification of the bone ground substance in the vicinity of the vessels. Normally the condition of calcium equilibrium in the adult is undoubtedly an instance of dynamic equilibrium in which the decalcification that is constantly going on is balanced almost exactly by calcification which is also a continuous process. Normally the calcium ingested in food replaces the calcium lost from the bone in the normal process of bone metabolism. The calcium excreted represents, therefore, the excess of calcium ingested plus the calcium lost from the bone. In an adult animal in which calcium equilibrium has been attained, the amount ingested equals the amount excreted almost exactly. It must be understood, however, that the calcium equilibrium may be disturbed by the ingestion of certain electrolytes that may displace calcium from the bone or may so change

the composition of the circulating fluids as to favor the excessive solution of calcium from the bone. Should calcium be withdrawn from the diet, then a negative calcium balance would also develop and conceivably the bone in the vicinity of the vessels would become relatively decalcified. The remaining organic ground substance is then more susceptible to enzymic or cellular influences favoring its removal.

For obtaining histologic evidence of decalcification, only the ground disk methods are useful. Ground disks of bone fixed in formaldehyde show that enlargement of the vessel canals is accompanied by changes in the ground substance of the bone, particularly in the calcium salts which, in the region of the resorption, appear as large irregular, coarse granules. In ground disks of normal bone they appear as fine, regular granules.

The way in which the bone becomes decalcified and what part the vessels and granulation tissue that have invaded the vessel canals play are still matters of speculation. The direct ability of the endothelial cells of the blood vessels to resorb the bone has been advocated by many and recently particularly by Pommer,<sup>10</sup> but others have denied this. The way in which the ground substance is decalcified depends on the cause of the bone resorption.

That bone may be decalcified *in vivo* has been shown by the fact that dietary deficiencies may lead to its decalcification. Experimental osteoporosis due to calcium deficiency is a well known example. Bone may be quickly decalcified *in vivo* by the administration of acids or acid salts, while starvation will also lead to similar results. Histologic evidence of decalcification in these instances is supported by chemical analysis of the bone. These facts are recited to show that in certain conditions of bone resorption decalcification is present and apparently precedes the enlargement of the vessel canals by a variable time interval. The results obtained from a study of the chemical and dietary deficiencies of bone are to some degree applicable to a study of the resorption due to inflammatory diseases, bone tumors, etc. It seems that the resorption of bone under any condition is dependent on previous decalcification. In inflammatory diseases the increased blood flow to the bone may be associated with local changes in the hydrogen ion concentration. The blood plasma and lymph are so well buffered that changes in hydrogen ion concentration are not easily produced. Cellular metabolism however, occurs under conditions which suggest that different  $p_H$  concentrations may exist in different portions of the same cell. The recent work of Chambers with his microdissection technic has shown this. These changes may even be more extensive without being reflected in a lower plasma  $p_H$ . Such increased local acidity may result in the

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10 Pommer G. Ueber Osteoporose ihren Ursprung und ihre differentialdiagnostische Bedeutung. Arch f klin Chir **136** 1 1925

production of narrow zones of either complete or relative decalcification in the vicinity of the vessels. These narrow zones of decalcified organic matrix permit further enlargement of the vessel canals when they are removed. As the vessel canals enlarge, newly formed vessels and granulation tissue appear in them. The decalcified organic matrix is removed by tissue enzymes or by phagocytes in the granulation tissue. Just how this change in the  $pH$  is made is not known. It may be due to local disturbances in the carbon dioxide tension, to local lactic acid production or locally to deficient oxidation.

I have indicated that decalcification may be brought about by a number of agents, both local and general. The extent of the preliminary decalcification depends on the cause of the decalcification. Decalcification due to ingestion of acids or acid salts or calcium deprivation may be of much greater extent than the decalcification due to local inflammatory conditions. The slow removal of the decalcified organic matrix accounts for the histologic evidences of calcium deficient bone as demonstrated by the osteoid borders in bone stained with eosin or carmine after Muller fluid decalcification. In such instances, there is a definite and prolonged time interval between the appearance of the calcium-poor zone and the removal of the calcium-poor organic matrix. In the more acute inflammatory conditions with local decalcification, the progress of the decalcification and the aggressiveness of the resorptive reaction may be so closely interrelated in time that no sooner is the bone decalcified than the decalcified matrix is removed. Under such conditions, clearcut histologic evidences of preliminary decalcification may be lacking. Even in these conditions, however, ground disks of undecalcified bone show that there is a change in the calcium salts in the vicinity of resorption, and that preliminary decalcification takes place in inflammatory diseases.

Volkmann's canals are produced in the same way. Between existing vessel canals local areas of decalcification appear which become vascularized. The appearance of threadlike cracks in the ground substance is associated with a loss of calcium along the path of the crack. The crack rapidly enlarges and grows in length, and gradually increases in width, beginning at the base which is at the haversian canal. An elongated, triangular passage is thus produced. The borders of the canal at this stage are irregular and toothed, and the canal is vascularized, but the vessel is preceded, according to Pommer,<sup>11</sup> by some connective tissue which seems to play a part in the opening of the crack. A Volkmann canal may become as wide as a normal haversian canal. Volkmann believed that the new canals resulted from the disintegration of bone

11 Pommer G. Untersuchungen über Osteomalacie und Rachitis. Leipzig F. C. W. Vogel 1885. Ueber den Begriff und die Bedeutung der durchbohrenden Knochenkanäle. Ztschr. f. mikr. anat. Forsch. 9:540, 1927.

ground substance and that lacunae and canaliculi of the bone cells rarely played a part in their production. Occasionally lacunae of the bone cells might be seen opening on a canal, but this happened only when a lacuna lay in its path. Volkmann recognized that the canals were vascularized by vessels coming from the existing haversian vessels.

*The Relation of Bone Cells to Vascular Resorption*—The possibility that the bone itself is not entirely passive in resorption deserves more attention. Virchow long ago called attention to the changes in the bone cells and lacunae in resorption and believed that Howship's lacunae were produced as a result of local disintegration of the bone. Others have even derived the Volkmann canals from lacunae and canaliculi of the bone cells.<sup>12</sup> In inflammatory resorption, I, like many others, have frequently noted enlargement of bone cell lacunae, degeneration of the bone cells and confluence of bone cell lacunae. Although these changes occur, I do not believe they result in the formation of Volkmann's canals. They have no direct relation to vascular resorption.

#### OSTEOCLASTIC RESORPTION

Probably much more has been written about the resorption of bone by osteoclasts than about any of the other phases of bone resorption. Though there are those who do not ascribe functional significance to the osteoclasts, the majority opinion accepts the resorptive ability of these cells as proved. Even those who accept the resorptive powers of the osteoclasts, however, differ as to the extent and importance of this activity. Some merely acknowledge that the osteoclast can resorb bone, while at the other extreme many declare that all resorption of bone is accomplished by osteoclasts. I am convinced that the osteoclasts are capable of resorbing bone, but I do not expect to find resorption by osteoclasts in all bone no matter what the basis for the resorption. I have seen extensive resorption of bone in the absence of osteoclasts. Such observations do not mean that osteoclasts have no bone-resorbing powers, but merely that in certain types of resorption of bone osteoclasts play a negligible role. Osteoclasts may be absent or they may apparently dominate the resorptive picture. Their presence or absence depends on the cause and the course of the resorption and they are merely an expression of the way in which the tissues are reacting to a stimulus. Osteoclastic resorption when present is always associated with other resorbing processes and it may come into prominence when vascular resorption is not aggressive. In conjunction with resorption of bone by osteoclasts with the resultant formation of Howship's lacunae, so many

12 Rindfleisch G. E. Pathologische Gewebelehre, ed. 5. Leipzig: Wilhelm Engelmann, 1878. Thierfelder F. A. Atlas d. pathol. Histologie. Leipzig: Fischer, 1876.

associated phenomena must be discussed, that the large amount of space devoted to osteoclastic resorption often gives an erroneous impression concerning its importance in pathologic resorption.

The process of resorption of bone by osteoclasts, resulting in the formation of Howship's lacunae, is known as lacunar erosion. Howship's lacunae appear on the periosteal or endosteal surfaces of the bone and less frequently on the walls of the vessel canals. They vary in form, but generally tend to be hemispherical depressions measuring from 30 to more than 100 microns in their greatest diameter. In or near these depressions, osteoclasts are frequently seen. These cells were first distinguished from the megakaryocytes of the bone-marrow by Robin<sup>13</sup>. Koelliker was the first to discuss the cause and effect relationship between osteoclasts and Howship's lacunae. Koelliker described them in the normal, physiologic resorption of growing bone, while Wegner<sup>14</sup> soon after discussed the presence of osteoclasts in the Howship's lacunae of pathologic bone. In certain parts of the normal growing skeleton where there is marked resorption, particularly in the jaw, osteoclasts and Howship's lacunae are present in large numbers, which is also true for certain pathologic conditions in which the resorptive process is slow and progressive.

The way in which the Howship's lacunae are formed has raised long and interesting discussions. Whether they are formed by the osteolytic activity of the osteoclast or whether these cells simply phagocytose the bone which has undergone a primary change will be discussed later. However, it is important to recognize that changes in the bone brought about by chemical and physical influences may lead to its softening, so that the bone may become more subject to cellular encroachment, or else, such changed bone may actually separate off, resulting in gouged out surfaces.

A discussion of the numerous aspects of osteoclastic resorption is necessary to show the development of the knowledge concerning these cells. When they are present in resorption they produce such a striking impression that attention is immediately directed toward them. So many conflicting reports concerning their origin, formation and function are current that a review is indicated with the perspective that osteoclasts are only a part of the process of resorption.

*Origin*—Different opinions have been expressed as to the cells from which the osteoclasts originate, the conclusions having been drawn from a variety of material. Their origin has been traced from the

13 Robin, C. P. Sur l'existence de deux especes nouvelles d'elements anatomiques qui se trouvent dans le canal medullaire des os, *Compt rend Soc de biol* 1 149, 1849.

14 Wegner, G. Myeloplaxen und Knochenresorption, *Virchows Arch f path Anat* 56 524 1872.

mature or embryonal connective tissue of the marrow from osteoblasts, bone cells and from the vascular or lymphatic endothelial cells. In view of the increased knowledge concerning the circulating mononuclear leukocytes and the wandering large mononuclear phagocytes of the tissues, their relation to osteoclast formation must be considered. The difficulty in tracing the origin of the osteoclasts in mammals is the fact that their formation is rapid, so that in fixed preparations it is difficult to find transition stages.

**Origin from Embryonal Connective Tissue** Koelliker, Morison,<sup>15</sup> Jackson,<sup>16</sup> Dantschakoff<sup>17</sup> and Maximow<sup>18</sup> traced the origin of the osteoclasts in fetal bone to the enlarged reticulum or embryonal connective tissue cells of primary bone-marrow. Jackson described their origin from the reticulum cells of the primary marrow through mitotic division of the nuclei without protoplasmic division. Dantschakoff and Maximow also traced the origin from these cells, but they believed that osteoclasts arise as a result of the confluence of these cells without nuclear division. According to Maximow, the giant cells at first remain in contact with the adjacent embryonal connective tissue by fine anastomotic processes, but these soon disappear. The number of nuclei in these first osteoclasts is usually between three and ten and the osteoclasts have irregular shapes. Morison expressed the belief that they may arise from the embryonic connective tissue by either multiplication or confluence. Jordan<sup>19</sup> recently confirmed Maximow's observations except that occasionally he observed mitotic division of the nucleus in the early stages. Arey<sup>20</sup> also held that in the earliest stages of bone development, and to a lesser extent in the later stages, osteoclasts apparently arise from the confluence of primitive connective tissue cells of the marrow. It seems then definitely proved that in fetal bone the osteoclasts arise from embryonal connective tissue, probably solely by confluence of these cells.

My studies of fetal bone are confirmatory of such an origin. In a number of young fetuses, I observed osteoclast formation from the

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15 Morison, A. Bone Absorption by Means of Giant Cells, *Edinburgh M J* **19** 305, 1873.

16 Jackson, C M. Histologie und Histogenese des Knochenmarkes, *Arch f Anat u Physiol*, 1904, p 33.

17 Dantschakoff, V. Entwicklung des Blutes und Bindegewebes bei den Vögeln, *Anat Hefte* **37** 471, 1908.

18 Maximow, A. Experimentelle Untersuchungen ueber die entzündliche Neubildung von Bindegewebe, *Beitr z path Anat* **32** 573 1902, Untersuchungen ueber Blut und Bindegewebe, *Arch f mikr Anat* **76** 1 1910-1911.

19 Jordan, H E. Further Evidence Concerning the Function of Osteoclasts, *Anat Rec* **20** 281, 1921.

20 Arey, L B. The Origin, Growth and Fate of Osteoclasts and Their Relation to Bone Resorption. *Am J Anat* **26** 316, 1920.

embryonal connective tissue surrounding vascular sprouts which were invading the capsules of degenerating cartilage cells. Osteoclasts that appeared in the primary marrow spaces in connection with the trabeculae of primary bone also could be traced to the mesenchymal connective tissue. Osteoblasts are developed from this same mesenchymal connective tissue (fig 12).

**Origin from Mature Connective Tissue** Von Rustizky<sup>21</sup> described the origin of the osteoclasts from mature connective tissue. By that he probably meant the fibroblasts. His conclusions were drawn from experiments on rabbits and from a large amount of pathologic material. He described two types of osteoclasts, fixed and wandering. An origin from mature connective tissue cells (fibroblasts) seems to be contradicted

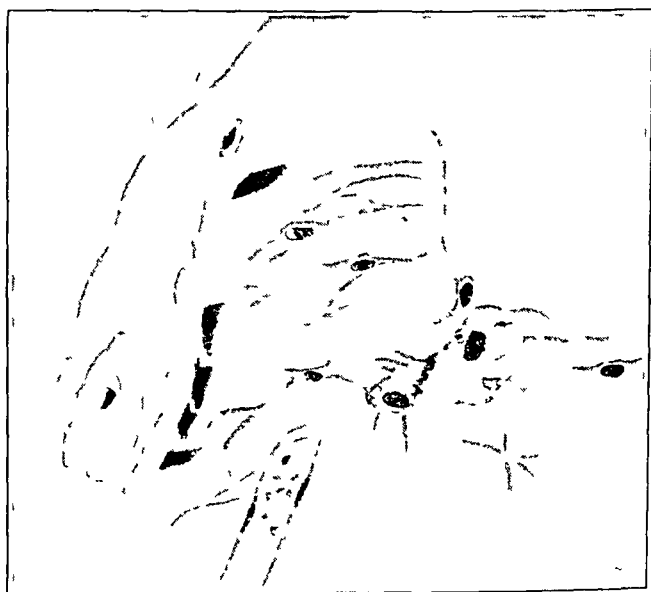


Fig 12—Camera lucida drawing of a primary trabecula lined by some osteoblasts. To the right a young osteoclast is seen forming by fusion of embryonal connective tissue. Some of the cells making up the osteoclast are still attached to the surrounding mesenchymal connective tissue by processes.

by the latest concepts of the connective tissues, which consider the fibroblasts as highly differentiated cells incapable of undergoing transformation into foreign body or inflammatory cells. Rustizky's views were in harmony with the ideas then prevalent concerning the origin of the giant cells in general. The theory that giant cells arose from fixed connective tissue cells originated with Virchow. This conception still has some adherents. Lubarsch,<sup>22</sup> as recently as 1923 mentioned that

21 Von Rustizky, J. Untersuchungen ueber Knochenresorption und Riesen zellen. Virchows Arch f path Anat 59:202, 1874.

22 Lubarsch, O. Entzündung. In: Aschoff, Ludwig. Pathologische Anatomie. Jena: Gustav Fischer, 1923, vol 1, p 556.

most of the giant cells in inflammatory granulation tissue were derived from fixed connective tissue cells

**Origin from Osteoblasts** Assuming that osteoclasts are derived mainly or entirely from mesenchymal cells during the embryonal life, it is important to discuss their mode of origin in later life in normal and in pathologic bone

Many of those who concede the origin of the earliest osteoclasts from embryonal connective tissue, nevertheless believe that in older bone or in diseased bone the osteoclasts are formed from osteoblasts. Even Koelliker, who is quoted as having formulated the osteoblastic theory of osteoclast formation, admits that during the erosion of the cartilaginous skeleton he saw pictures that indicated the origin of some of the osteoclasts from mesenchymal connective tissue. Others have derived all osteoclasts from osteoblasts. The condition of the osteoblasts at the time of osteoclast formation has been variously stated and there has also been a difference of opinion as to whether osteoclasts are formed from osteoblasts by a process of confluence or by mitosis.

Koelliker maintained that osteoclasts arise almost exclusively from osteoblasts and attain their multinuclearity by repeated nuclear divisions. Pommer<sup>23</sup> also believed that osteoblasts were capable of producing osteoclasts, as Koelliker described, but he did not believe that they arose exclusively from osteoblasts. Howell<sup>24</sup> believed that giant cells in general were formed by fusion of smaller cells in consequence of too rapid growth and that osteoclasts in particular were probably formed by fusion of closely packed osteoblasts which were forced to coalesce. Allen expressed the belief that while in the early stages of bone development and to a certain extent in later stages osteoclasts apparently arise from the confluence of mesenchymal and connective tissue cells of the marrow the chief source of osteoclasts is from old osteoblasts and bone cells. He stated that the depleted basophilic osteoblasts coalesce to form multinucleate masses. These syncytial elements become typical osteoclasts when their cytoplasm assumes oxyphilic properties. He found intermediate tinctorial and transitional stages. On the other hand Jordan, while tracing most of the osteoclasts from the marrow reticulum found that during later stages osteoclasts also arise from young slightly differentiated osteoblasts by fusion.

While these authors admit an origin of osteoclasts either entirely or partly from osteoblasts there is no unanimity of opinion as to whether the osteoblasts are depleted or physiologically active or whether

23 Pommer G. Ueber die Osteoblastentheorie. Virchow's Arch f path Anat 92: 296 1883

24 Howell W. H. Observations Upon the Occurrence, Structure and Function of the Giant Cells of the Marrow. J Morphol 4: 117 1890 1891



the process is one of nuclear division without division of the protoplasm or one of cell confluence

Studying many sections from a variety of material, I have not found convincing evidence of the origin of osteoclasts from osteoblasts. While I have frequently seen large clumps of osteoblasts on trabeculae, generally these clumps were made up of cells which always maintained their individuality. Where there were evidences of nuclear and cytoplasmic degeneration in these cells, no definite evidence of fusion was observed. In specimens of adult bone decalcified in Muller's solution and stained with eosin and methylene blue, the cytoplasm of the individual osteoblasts and clumps of osteoblasts was always basophilic, while the osteoclasts, no matter how small and no matter how few the nuclei, always had acidophilic cytoplasm. My studies lead me to reject the conception that osteoclasts are formed from osteoblasts, and this holds for both embryonal and adult bone.

**Origin from Bone Cells** In regard to the origin of osteoclasts from bone cells, Bredichin<sup>25</sup> stated that the giant cells are a stage in the process of the transformation of bone into marrow and granulation tissue. A similar view was held by Kassowitz,<sup>26</sup> who, however, believed that at first there was an increased vascularization of the bone and decalcification, following which the bone cells proliferated to form giant cells. Loewe<sup>27</sup> believed that the osteoclasts arise from bone that was decalcified after its separation from the main bone mass. Finally, these osteoclasts break up into as many individual cells as there are nuclei, and disperse themselves in the bone-marrow. Lang<sup>28</sup> also believed that the giant cells arise mainly from bone cells. While bone cells may be taken up by osteoclasts, several authors having actually observed their phagocytosis by giant cells, an origin of osteoclasts from bone cells seems untenable.

**Origin from Vascular Channels** Wegner observed a close association between osteoclasts and blood vessels in pathologic bone. He believed that in bone resorption osteoclasts arise by proliferation of the vessel wall, and that these osteoclasts erode the bone as they are proliferating. Wegner is not clear as the details of such an origin. He does not state whether these cells arise from the lining endothelial cells or from the perivascular endothelium, or from the muscular and connective

25 Bredichin, J. Ueber die Bedeutung der Riesenzellen im Knochen, *Centralblatt f. d. med. Wissensch.* 5 563, 1867.

26 Kassowitz, M. Die normale Ossification und die Erkrankungen des Knochensystems, *Med. Jahrb.*, 1879, pp. 145 and 293.

27 Loewe, L. Ueber die Umwandlungen der Osteoklasten im Knochenmark nebst Bemerkungen ueber Knochenwachstum, *Arch. f. mikr. Anat.* 16 618, 1879.

28 Lang, F. Untersuchungen ueber die ersten Stadien der Knochenentzuehung, *Med. Jahrb.*, 1871, p. 34.

tissue elements of the wall. Others, among them Maas,<sup>29</sup> expressed an intimate relation between the osteoclasts and the vessel walls, though they did not state that the cells are actually derived from the vessel walls.

*The Foreign Body Giant Cell Conception of Osteoclasts*—Throughout the literature on osteoclasts the idea frequently recurs that osteoclasts are related to the giant cells found in a wide variety of conditions. Mallory<sup>30</sup> made a definite statement to that effect. Haythorn,<sup>31</sup> in a recent review of the subject, accepted this point of view and he said that most modern writers group the Langhans' cell of tuberculosis, the common foreign body giant cell and the osteoclasts as one cell type which forms in response to a stimulus and which varies morphologically only with local environmental influences. The view that the osteoclasts are functionally and genetically related to foreign body giant cells is an important conception and one that is helpful in explaining the origin of osteoclasts in pathologic resorption during adult life. It seems logical that injured, decalcified or dead bone that shows no regenerating tendency becomes essentially a foreign body, and the cells in contact with it try to remove it.

To enter into a detailed discussion of the origin of the foreign body giant cell as a basis for the understanding of the origin of the osteoclast of later life would take me too far afield. Moreover, this has recently been well down by Haythorn. The opinion is that foreign body giant cells are derived from the mononuclear leukocytes of the circulation and wandering cells of the tissues. Whether mononuclear leukocytes arise from vascular or lymphatic endothelium (Mallory), whether they are transformed cells of the marrow (Sabin) or circulating blood cells (Maksimow), or whether they come from the reticulo-endothelial system (Aschoff) and what their connection is with the wandering cells of the tissues are problems that have not been settled. Whatever the exact origin of the wandering large mononuclear phagocyte of the tissues may be, and whether they represent a single specific cell or a group of allied cells, these cells and the mononuclear leukocyte are concerned in the formation of the foreign body giant cell and consequently the osteoclast of later life.

The relation of the osteoclast to the foreign body giant cell has been stressed, and I believe must be accepted. From a study of the literature and from my own observations, it appears that the osteoclast in embryonic life is derived from the mesenchyme, and that in later life, under both normal and pathologic conditions, the osteoclast is

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29 Maas, H. Ueber das Wachstum und die Regeneration der Roehrenknochen. *Arch f klin Chir* 20 718, 1877.

30 Mallory, F. B. Giant Cell Sarcoma. *J M Research* 19 463, 1911.

31 Haythorn, S. R. Multinucleated Giant Cells, *Arch Path* 7 651 (April) 1929.

a reactive cell arising by fusion of the resting wandering cells of the tissues supplemented by the mononuclear cells of the circulation. It seems to me that the theory of an origin by osteoblastic fusion or proliferation must be abandoned. Osteoblasts and bone cells may be present in osteoclasts, if so, they are present by virtue of phagocytosis.

*Morphology*—The appearance of the individual osteoclast varies considerably. The osteoclast may be either small or large and may contain a few or as many as 100 nuclei. Large, fully developed osteoclasts are elongated, flat, multinucleated cells of irregular shape, without a definite limiting membrane. Koelliker recorded their maximum size in the new-born infant as from 43 to 91 microns in length, from 30 to 40 microns in width, from 16 to 17 microns in thickness, and with as many as fifty or sixty nuclei. Arey found the measurements in the embryonal pig to run as high as from 65 to 105 microns, with a nuclear count of about 125. Smaller mature osteoclasts may contain as few as five nuclei or less and be no more than from 6 to 10 microns in the largest diameter. The first osteoclasts formed during embryonal bone formation usually have between three and five nuclei. Osteoclasts often fuse to form large syncytial masses.

Some osteoclasts have been described with simple, branched or pseudopod-like processes, and Dantschakoff, Maximow and Arey believed that osteoclasts were capable of ameboid motility, but Koelliker failed to confirm ameboid motility in living osteoclasts, examined on a warm stage. That they are capable of moving about is evident from the facts that they frequently are outside of the Howship's lacunae, and that they may be seen entering capillary vessels (fig. 13).

The cytoplasm of osteoclasts encountered in adult or in pathologic bone is strongly acidophilic. While some have observed osteoclastic cytoplasm in all tinctorial stages from basophilic to acidophilic, I have not observed a cell that I could with certainty call an osteoclast, except in embryonic life, that contained any but acidophilic cytoplasm. The cytoplasm is granular, sometimes coarsely so. When stained according to Foot's<sup>32</sup> modification of the Bielschowsky-Maresch silver impregnation method, the cytoplasm of osteoclasts contains large, coarse, black granules (fig. 14). A variable number of vacuoles is present, but whether these are fat has not been definitely proved.

The nuclei are round or obliquely round and tend to be pyknotic, especially in the older, apparently degenerating forms. One or two nucleoli may be seen in varying positions. Some nuclei appear shrunken or folded, but convincing amitotic stages have not been observed by Maximow, Arey and others. Koelliker reported finding

<sup>32</sup> Foot, N. C. Chemical Contrast Between Collagenous and Reticular Connective Tissue. *Am. J. Path.* 4: 525, 1928.

some division figures, but most of those who focused their attention on this point were unable to confirm the observation Maximow, though not denying the possibility stated that he never observed mitotic or amitotic division figures in the material he examined. In pathologic material, I never observed mitotic division figures.

Certain osteoclasts exhibit a brush border along the edge in apposition with the bone. Koelliker and Wegner were among the first to make this observation. Arey observed this particularly in the osteoclasts of cattle. Maximow even observed such borders on some of the foreign body giant cells. In dogs suffering from experimental osteoporosis, I have occasionally observed such borders. This border

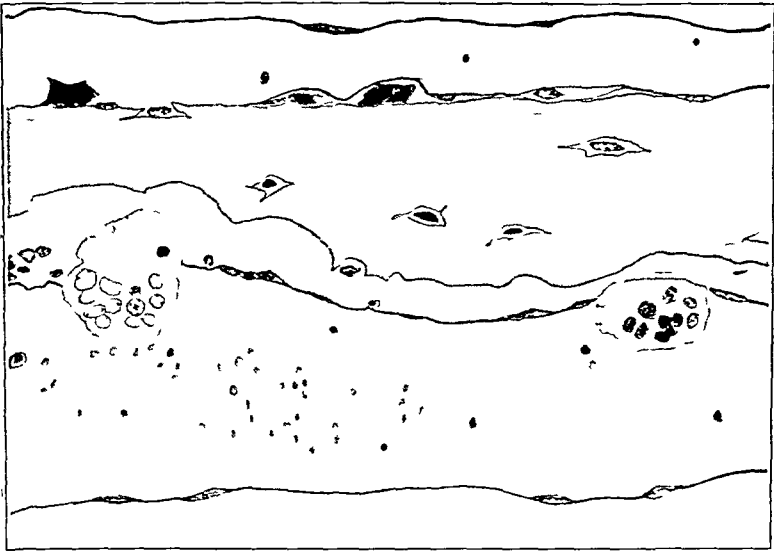


Fig. 13—Camera lucida drawing showing a spongy trabecula from the marrow cavity of a rib of a dog suffering from osteoporosis. The lower surface of the trabecula shows resorption; osteoblasts having disappeared. Some Howship's lacunae and an opened bone cell lacuna are seen. One osteoclast is seen in, and another is seen entering a dilated capillary adjacent to the trabecula. Magnification about 600.

stains more intensely than the rest of the cell and may be finely striate or composed of coarse elements. Some osteoclasts have a fringed or toothed appearance while others are observed with fibers and fibrils the free edges of which extend from the cell and are in contact with the surrounding tissues.

*Function*—In spite of some negative statements in the literature it may be accepted that osteoclasts are capable of removing bone. I mean to include here their ability to erode bone directly as they sometimes appear to be doing when they are in Howship's lacunae and also

the ability to phagocytose dead bone. But how important this function is, in resorption of bone, is open for discussion. Koelliker was the first and most persistent exponent of their bone-destroying function. He believed that their presence in the Howship's lacunae of resorption surfaces demonstrated this function beyond controversy. Among the many who have subscribed to this view were Wegner, Morison, Jackson, Maximow and Jordan. Mallory even suggested that the erosion of bone may be accomplished mechanically by the brush border of the osteoclast. Schaffer<sup>33</sup> likewise held that osteoclasts have a bone-destroying action. Jordan described the presence of small spicules of bone within some osteoclasts, which he believed were phagocytosed. Using Foot's modification of the Bielschowsky-Maresch silver impregnation technic, I have also observed osteoclasts containing fragments of bone. These fragments stained like the collagen fibrils of the bone (fig 15).

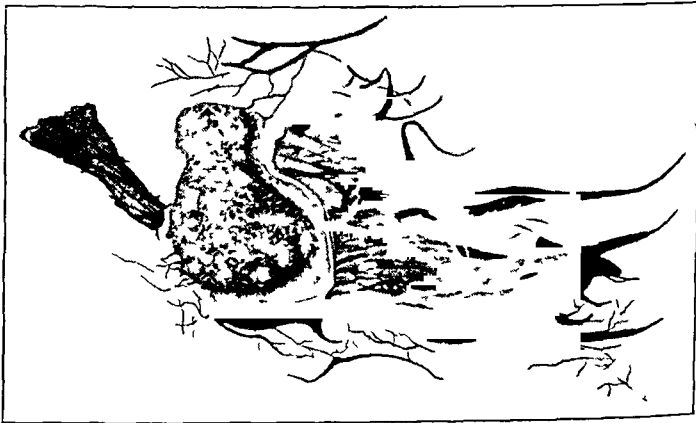


Fig 14—High power camera lucida drawing of part of a trabecula from the medullary cavity of an osteoporotic rib of a dog. A deep Howship lacuna is seen containing an osteoclast which fits snugly into the lacuna. The osteoclast shows numerous coarse dark granules. Paraffin section, Bielschowsky-Maresch silver stain.

In spite of much evidence in favor of either a phagocytic or an osteolytic function of the osteoclasts, some definite denials of such function have appeared. Strelzoff<sup>34</sup> did not believe that osteoclasts could resorb bone. Ziegler<sup>35</sup> doubted the resorptive function of osteoclasts, because he believed that the osteoclasts seen in numerous bone conditions were genetically unrelated. Howell opposed the probability of

33 Schaffer, J. Die Verknöcherung des Unterkiefers und die Metaplasiefrage. *Arch f mikr Anat* 32:266, 1888.

34 Strelzoff, Z. J. Ueber die Histogenese der Knochen, *Unters aus d path Instit zu Zurich*, Herausg v C Eberth, Leipzig, 1873.

35 Ziegler, E. Ueber Proliferation, Metaplasie und Resorption des Knochengewebes, *Virchows Arch f path Anat* 73:355, 1878.

osteolytic function, believing that the formation of osteoclasts in embryonic life or in pathologic conditions was accidental owing to rapid growth and fusion of the cells. Lewis<sup>36</sup> thought that there was no satisfactory evidence that the osteoclasts were active causes of bone destruction, and believed that they were degenerating cells. Arey recently stated that only indirect and insufficient evidence points to osteoclasts as active, specific agents of bone resorption. To him they are merely degenerating, fused osteoblasts. Arey would attribute to them the capacity of phagocytosis but not osteolysis. Furthermore, he stated that the mere presence of cytoplasmic inclusions within an osteoclast by no means indicates that the latter was responsible for the dissolution of the material ingested.

Arey takes issue with those who use "osteolytic" as a term interchangeable with "phagocytic." In the true sense, osteolysis by osteo-

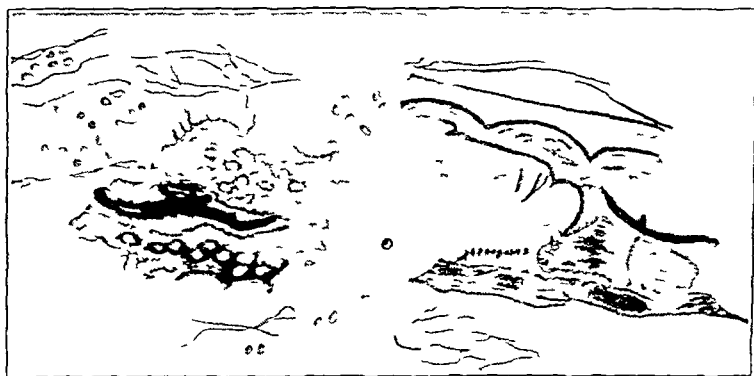


Fig 15—High power camera lucida drawing of a trabecula from the marrow cavity of a dog suffering from osteoporosis. On the right there is a Howship's lacuna with a fringed border. On the left is an osteoclast containing a large piece of phagocytosed bone. Paraffin section, Bielschowsky-Maresch silver impregnation.

clasts implies the direct dissolution of unchanged bone by these cells. Phagocytosis of the bone implies the removal of changed bone. Whether osteoclasts are capable of osteolysis or phagocytosis of bone depends on whether the osteoclasts dissolve the inorganic salts before they remove the organic matrix. There is no direct way of proving this, and it seems that most authors have not distinguished between osteolysis and phagocytosis in regard to bone. If such a distinction is to be made, then the function of the osteoclast is certainly that of a phagocyte. Whether it can also dissolve the bone directly cannot be answered at present. On the basis of available knowledge it would be better to think of the

<sup>36</sup> Lewis, F. T. A Text-Book of Histology, Philadelphia: P. Blakiston's Son & Company, 1913.

osteoclasts as bone resorbers rather than as bone dissolvers. Large osteoclasts may be observed within the blood vessels of the marrow. That such gain admittance and do not arise in situ from the endothelium is supported by their degenerated appearance. I have observed such osteoclasts in the marrow vessels, and believe that much of the bone which they phagocytose is removed in this way.

The observations refuting the resorptive ability of osteoclasts are that Howship's lacunae may be seen without osteoclasts, and often in inflammatory diseases there may be extensive resorption of bone also without osteoclasts, especially in acute fulminating osteomyelitis. These observations do not prove that osteoclasts are not resorbing agents but serve only to emphasize what I have said before, that there are other types of bone resorption besides the osteoclastic type. From my experience it appears that in the more acute inflammatory diseases of bone, erosion by osteoclasts is unimportant. On the other hand, in the less acute inflammatory processes osteoclasts are numerous and seem to be playing a significant part in the resorption.

In summary, I believe that osteoclasts are capable of resorbing bone but they are of secondary importance in resorption of bone. Whenever osteoclasts are resorbing bone, there is also vascular resorption, but vascular resorption may under certain circumstances be so extensive that it may completely overshadow osteoclastic resorption. Osteoclastic resorption is more likely to be seen in the slower resorptive processes and since osteoclasts in later life are formed like other foreign body giant cells, they occur more frequently in chronic inflammations. I believe that they are active aggressive cells capable of removing the bone. The bone at the time of its removal by osteoclasts is undoubtedly decalcified, but how much, if any, of the decalcification is produced by the osteoclasts cannot be answered.

*Fate*—Most opinions pertaining to the fate of osteoclasts either uphold the theory of their transformation into other cellular elements or suggest their total destruction, or admit both possibilities. Ribbert believed that the osteoclasts disintegrated and disappeared like the giant cells of giant cell tumors. Bredichin thought them to be transitional stages in the transformation of bone tissue into marrow and granulation tissue. Wegner believed that they became transformed into spindle connective tissue cells, but, observing that some had passages, was led to speculate as to whether new blood vessels might arise from osteoclasts. Koelliker suggested that after their resorptive activity increased the osteoclasts may divide into osteoblasts and resume bone formation but he found no definite proof of this. Morrison denied it. Koelliker also considered their degeneration or transformation into connective tissue or marrow cells. Jackson and Maximow have upheld the fragmentation of osteoclasts in the embryo into detached cells which

became indistinguishable from the reticulum of the marrow. But in adults according to Maximow, the osteoclasts never revert in this way always undergoing degeneration and disappearing. This also holds true to some degree in the embryo and Jordan believed that osteoclasts of the embryo disappear by degeneration. Most likely osteoclasts finally either degenerate locally or enter blood vessels and are removed in this way.

*Howship's Lacunae Their Relation to the Osteoclasts*—Howship's lacunae always appear on the surfaces of bone, arising subperiosteally or under the endosteum or on the surface of the vessel canals but they do not appear within the substance of the bony trabeculae or lamellae. According to Koelliker, the lacunae are smooth and have sharp borders and are bordered by normal bone. The lacunae are sometimes rounded and sometimes irregular. Pommer described fringed or brushlike borders on some lacunae produced by fibrils or fibril bundles which remained preserved on dissolution of the ground substance. He believed that he could trace them to the fibrils of the surrounding lamellae. In sections stained by Foot's modification of the Bielschowsky-Maresch technique I have frequently observed such lacunae (fig. 15). Pommer observed osteoclasts with finely fringed borders, matted with the brush borders of lacunae. The osteoclasts may conform to the shape of the lacunae but their form is often more varied than that of the lacunae. The frequency with which osteoclasts are related to lacunar erosion is difficult to judge, because it is known that with the cessation of the resorptive activity the osteoclasts disappear and connective tissue marrow or granulation tissue replaces them. Then new bone may be deposited on the walls of the lacunae by osteoblasts which line them. When the lacunae no longer contain osteoclasts, Pommer believes that resorption has ceased. It is known that lacunae occur in resorbing bone without containing osteoclasts. The cause and effect relationship between Howship's lacunae and osteoclasts is generally admitted (fig. 16) but the manner in which the lacunae are formed and the part that osteoclasts play in their formation seem never to have been definitely settled.

In regard to the part that the ground substance plays in the formation of Howship's lacunae Pommer<sup>22</sup> has often stated that it is entirely passive and that lacunar resorption is in no way dependent on preparatory decalcification of the ground substance. According to him lacunar erosion takes place the same way in calcium-free and in normal bone. Von Recklinghausen<sup>37</sup> has shown conclusively that in osteomalacia the resorption of bone is preceded by the removal of calcium. The extent of the preliminary decalcification of the ground substance

<sup>37</sup> Von Recklinghausen F. Untersuchungen ueber Rachitis und Osteomalacie. Jena Gustav Fischer 1910.



in resorption of bone due to inflammation is not conclusively settled, though Volkmann believes that there is evidence of such a process, and Ribbert thinks that it occurs in all normal pathologic resorption.

I believe that in the formation of Howship's lacunae, preliminary decalcification plays an important role. A Howship lacuna is probably formed as follows. Resorption is initiated when bone formation ceases. Then a decalcifying influence is exerted on the bone which varies with the etiologic factor of the resorption. Just what decalcifies the bone is not known. The various possibilities were discussed under vascular erosion. It may be changed  $p_{H}$  or local lactic acid production or changed local carbon dioxide tension. Whatever this factor is, it exerts an

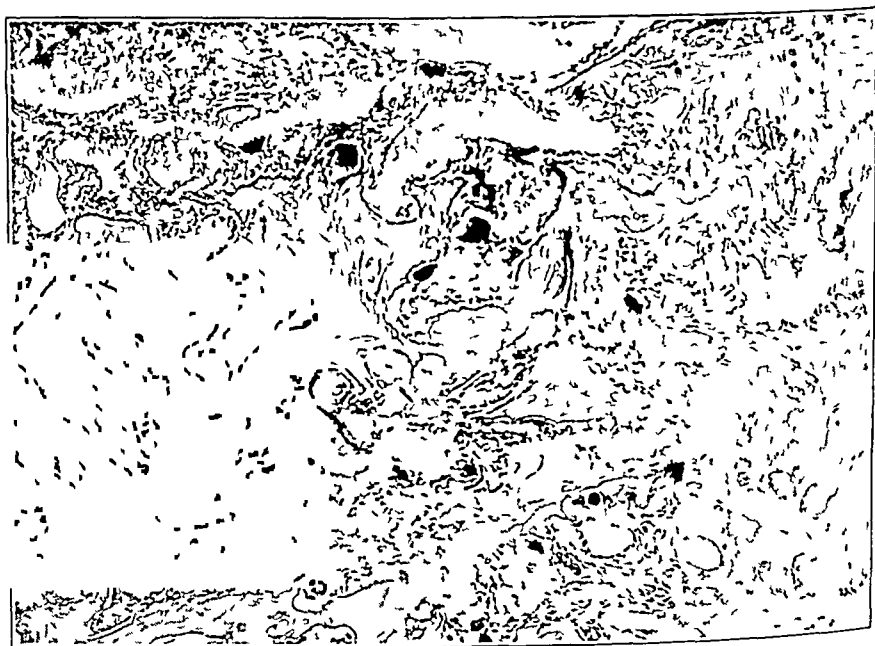


Fig. 16—Section through bony callus of a healing fractured rib in a dog suffering from osteoporosis. Numerous osteoclasts are seen occupying Howship's lacunae in the process of reconstruction of the callus. Paraffin section, Muller decalcification, eosin and methylene blue stain,  $\times 75$ .

effect on the surfaces of the spongy trabeculae, just as it does on the walls of the haversian canals or anywhere else. Osteoclasts arising locally as reactive, resorptive cells then remove the decalcified bone. The stimulus to osteoclast formation varies with the resorptive processes. I doubt whether the osteoclasts themselves exert a dissolving influence on the bone before they remove the ground substance, but unequivocal evidence in either direction is unavailable.

*The Relation of Howship's Lacunae to Bone Cells*—In regard to the behavior of the bone cells and their processes in lacunar resorption, many believe that they are entirely passive and that the cells in closed

lacunae never show changes. Opened bone cell lacunae either are empty or contain cells not much altered. The bone cells may degenerate and are then phagocytosed by the osteoclasts. On the other hand, some believe that the bone cells may produce lacunar resorption and Howship's lacunae. Virchow was the originator of this conception and described the formation of Howship's lacunae as due to fatty metamorphosis of the bone cells, followed by their enlargement and nuclear division. Concomitantly with the nuclear division changes in the ground substance occur and spherical or elongated masses of the ground substance are split off and continue to disintegrate into granules leaving cavities the Howship's lacunae. Virchow had numerous supporters of his view. It is, of course, true that in inflammatory diseases of bone regressive changes, such as fatty metamorphosis and degeneration of the bone cells occur, but not constantly. While Virchow's theory has had supporters, a greater number of workers have felt that the progressive changes in the bone cells were related to lacunar resorption because they proliferated to form giant cells which produce the Howship's lacunae.

That the bone cells play an active part in resorption was denied by Koelliker, Billroth and Volkmann, who have often demonstrated experimentally that bone cells in the vicinity of Howship's lacunae do not have enlarged cavities. However, the observation of Virchow that in resorptive processes the bone cell lacunae enlarge can easily be confirmed on examining bone from a variety of resorptive processes. The observation is more common when inflamed bone is examined. As I have stated, in some instances the appearance of lamellar bone may be so changed by the enlargement of Howship's lacunae that in a decalcified section stained with hematoxylin and eosin such bone may look like fiber bone. I have seen large spaces formed within the substance of spongy trabeculae by the coalescence of enlarged lacunae. Such observations are probably dependent on circulatory disturbances in the bone, possibly on thrombosis of vessels leading to the bone. I do not believe that degeneration of the bone cells and enlargement of the bone cell lacunae are important in the actual resorption of bone but such bone is more subject to resorption.

# LOCALIZED BULBAR CISTITIS (PONTILE) MENINGITIS FACIAL PAIN AND SIXTH NERVE PARALYSIS AND THEIR RELATION TO CARIES OF THE PETROUS APEX

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## I. FACIAL PAIN

Gradenigo syndrome of sixth nerve paralysis, associated with fifth nerve pain and a discharging ear has been the subject of numerous communications, the general trend of which would give the impression that the abductor paralysis results from pressure on the nerve either (a) by the petrosphenoidal (Gruber's) ligament as the nerve passes over the petrous apex secondary to swelling of the bone of the petrous apex or (b) it is the manifestation of a localized meningitis in the neighborhood of the nerve. In a few cases sixth nerve paralysis has been regarded as resulting from (c) neuritis of toxic origin.

The prognosis is generally regarded as favorable. All authors advocate the prompt opening of the mastoid when the neurologic symptoms appear early in the course of an otitis while in the cases in which the syndrome develops subsequent to the operation delay in further operating is advocated as both the paralysis and the pain usually disappear spontaneously.

## FATAL CASES OF GRADENIGO SYNDROME

Gradenigo pointed out that in many cases there was an associated extracranial abscess, and Sears,<sup>1</sup> in a compilation of the literature, found that in nearly 20 per cent of all the reported cases the patients died from an intracranial complication.

In spite of this high mortality, little attention has been paid to the possibility of the early recognition of the type of case in which meningitis develops although a mastoid operation may have been performed.

## OBJECTS AND METHODS OF INVESTIGATION

The first object of this communication and the dissections on which it is based was (1) to determine the various anatomic factors that may cause facial pain and sixth nerve paralysis in suppuration of the

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\* Presented in part before the combined Otolological Sections of the New York Academy of Medicine and the Philadelphia College of Physicians on April 27, 1927, and to the First International Congress D'Oto-Rhino-Laryngologie at Copenhagen, Aug. 1, 1928.

1. Sears, W. H. Orogenic Paralysis of the Abducens with Especial Mention of Isolated Palsy Associated with Irritation of the Gasserian Ganglion, *Trans. Am. Laryng. & Otol. Soc.*, 1925, p. 89.

petrous and meninges. For with the exception of Baldenweck—no attempt has been made to solve the problems presented by the Gradenigo syndrome—(a) why it occurs in one case of suppuration in the mastoid and not in another, as well as (b) what anatomic peculiarity excites a contralateral abductor paralysis—by the obviously direct method of studying the anatomic relationships of the petrous apex and its neighborhood as found in a succession of cadavers. (2) The second object is to apply the knowledge obtained from dissections to the clinical differentiation between the cases in which recovery occurs and those in which intracranial complications uniformly develop in order that the latter group may be promptly recognized and surgically attacked at an early date. It is only during the primary stage of the meningeal process that surgical intervention promises some measure of success in the admittedly large percentage (20 per cent) of cases which otherwise end fatally.

*Experimental Methods Employed in Anatomic Dissections*—The surgical anatomy described is based on the dissection of eight embalmed cadavers (placed at my disposal by Professors F. Lemaître and G. Rouhier of Paris). In seven cadavers, the (a) arachnoid prolongation surrounding the internal auditory meatus, or the (b) meshes of the arachnoid in the region of the posterior fossa just superior to the jugular bulb were opened, into which a solution of dye was introduced and from them allowed to diffuse by gravity through the spaces of the arachnoid.

*Anatomic Basis of Facial Pain and Sixth Nerve Paralysis*—During the dissection on the cadavers an effort was made to ascertain an anatomic basis for sixth nerve palsy and fifth nerve pain in the various types of osteitis, phlebitis and meningitis.

#### FACIAL PAIN IN SUPPURATIVE OTITIS DIAGNOSTIC OF MIDDLE FOSSA INVOLVEMENT

Facial pain in suppurative disease is diagnostic of middle fossa involvement because the gasserian ganglion and the other nervous elements that may contribute to the production of facial pain lie anterior to the tentorium. Posterior fossa inflammation does not cause facial pain, for although the sensory root of the fifth nerve is in the posterior fossa the periarachnoid prolongation surrounding it is so loose that pressure from inflammation of the bone of the posterior surface of the petrous or of the dura covering it cannot affect it. Even after the exit of the root through the ringlike opening in the tentorium above the superior

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2 Baldenweck, Louis. Étude anatomique et clinique sur les relations de l'oreille moyenne avec la pointe du rocher, le ganglion de Gasser et la sixième paire crânienne. Thèse de Paris, 1907-1908.

border of the petrous, the outer portion of the ganglion as well as its second and third branches lie free in the cerebrospinal fluid. The arachnoid prolongation extends halfway across the floor of the middle fossa, up to a line opposite the foramen spinosum. Dye introduced into the arachnoid spaces of the posterior fossa uniformly reaches this point. Suppurative leptomeningitis does not cause facial pain. It is only on its mesial side that the semilunar ganglion has dural adhesions. It is this freedom from pressure that explains the absence of facial pain in those cases of suppurative meningitis in which the bulbar cisterna is the seat of a firm exudate without involvement of the dura of the middle fossa.

Inflammation in the arachnoid irritates the tissue of the brain cortex and causes fever, headaches, restlessness, etc., but localized pain from irritation of the sensory nerves after they emerge from the brain is induced only by direct pressure, because immediately on coming in contact with the arachnoid, the sensory nerves acquire a surrounding sheath—a combination of mesoblastic and ectoblastic tissue—the sheath of Schwann.

*Facial Pain of Peripheral Not Central Origin*—When, however, that portion of the floor of the middle fossa, which is formed by the superior surface of the petrous pyramid internal to the eminentia arcuata, is the seat of inflammation either (a) the ganglionic portion of the trigeminus, (b) a branch or branches of the fifth nerve itself or (c) one of the sensory elements of the facial, glossopharyngeal, vagus or cervical nerves may be irritated. In suppurative inflammation the resulting localized facial pain is largely due to the intimate relation of these sensory nerves or their communications with the bone of the cranial base posterior to the sphenopetrous suture, in which region the dura is closely adherent to the bone.

#### PATHOLOGIC DISCREPANCIES BETWEEN CASES OF REferred AND DIRECT FIFTH NERVE PAIN

All cases of facial pain that disappears after the simple evacuation of the mastoid are probably caused from irritation of one of the sensory communications of the fifth and not of the trifacial nerve.

However, in cases of caries of the petrous apex, the resulting pain is probably occasioned by direct irritation of the semilunar ganglion or its first branch because of their dural adhesions, and this type of pain is not apt to be influenced by a mastoid operation.

(a) *Referred Facial Pain, Pain from Irritation of Sensory Nerve on the Floor of the Middle Fossa having Communication with the Fifth Nerve*—In cases in which the irritation originates from the external two thirds of the temporal bone—the middle ear, mastoid and

labyrinthine area (that is the area external to the outer lip of the gasserian ganglion)—the accompanying facial pain probably has nothing to do with the gasserian ganglion although referred to one or other of its branches, because of the overmastering command that the trifacial nerve has over the dura of the middle fossa

Irritation, then, of the sensory elements from congestion or edema of the cells in the superior surface of the petrous may occasion pain in one or other branches of the trifacial nerve, and this without involving the gasserian ganglion itself although both the facial and the glossopharyngeal nerves have communication with the gasserian ganglion (under which they lie) and with its dural covering from which it is difficult to separate the nerves by dissection

*Mechanism of Referred Facial Pain*—The anatomic requirements in nervous tissue necessary for the reference of pain from a visceral area to a body surface are (1) ganglion cell fibers carrying impulses toward the central nervous system from both a visceral region and a body surface located in proximity in the same sensory ganglion while sensory impulses from both sets of cells pass together to the brain (Head<sup>3</sup>), or (2) "impulses from afferent visceral fibers transferred to somatic ganglion cells in a dorsal root ganglion or its equivalent"

In man, the trifacial nerve assumes most of the sensory elements found in the facial, auditory, glossopharyngeal and vagus nerves of vertebrates possessing a lateral line nervous system, however Hunt<sup>4</sup> clinically and Larsell and Fenton<sup>5</sup> histologically have demonstrated that the great superficial petrosal of the facial and the small superficial petrosal from the glossopharyngeal nerves contain sensory fibers, and as both nerves lie in bony canals on the superior surface of the petrous any inflammatory swelling may cause a neuralgia from irritation

On the superior surface of the petrous, confined in bony grooves, is the geniculate ganglion of the facial nerve from which runs the great superficial petrosal and the great deep petrosal the latter with "myelinated fibers of the glossopharyngeal and unmyelinated postganglionic fibers from the superior cervical ganglia by way of the carotid plexus" Both unite to form the vidian which latter communicates with Meckel's (sphenopalatine) ganglion

Irritation of the superficial petrosal of the facial nerve may cause pain referred to the second branch of the fifth nerve because of the

<sup>3</sup> Herd H. The Pathology of Herpes Zoster. Brain 1893, vols 16 and 17

<sup>4</sup> Hunt Ramsay. Sensory System of the Facial Nerve and Its Symptomatology. J Nerv & Ment Dis 1909, vol 36

<sup>5</sup> Fenton R. A. Mechanism of Pain Transmitted in Certain Types of Otalgia. First International Oto-Rhino-Laryngological Congress, Copenhagen 1928  
Larsell and Fenton. Embryology and Neurohistology of Sphenopalatine Ganglion Connections. Tr Am Otol Soc 1928

communication of the great superficial petrosal through Meckel's ganglion which is attached to the second branch. Larsell and Fenton have demonstrated that the sensory fibers pass through the sphenopalatine without entering the ganglion itself.

Lateral to the hiatus, in which lie the gemulate ganglion and the superficial petrosal, there is a smaller canal for the lesser superficial petrosal which passes to the otic ganglion.

Irritation of the small superficial petrosal through its connection with the otic ganglion which is attached to the third may thus occasion a referred pain in the lower facial region.

(b) *Sensory Elements of the Glossopharyngeal Nerve*—The glossopharyngeal nerve in its intradural portions is probably a special sense nerve devoted to gustatory and secretory functions (Fay<sup>6</sup>), but its communicating fibers which ascend through the temporal bone and reenter the cranial cavity through Jacobsen's tympanic plexus to the small superficial petrosal and by the small deep petrosal and the carotid plexus in the floor of the middle fossa probably contain sensory elements. The great deep petrosal formed by the small deep petrosal and fibers from the carotid plexus and Jacobsen's plexus probably obtain their fibers from the petrosal ganglions.

*Muscular Involvement of the Fifth Nerve in Suppurative Lesions from Irritation of the Glossopharyngeal*—In suppurative disease, facial pain with trismus may follow irritation of the tympanic plexus of the glossopharyngeal (Jacobsen's) such as may be caused by a plug of cotton in the external canal of the middle ear causing a congestion of the deeper parts (Uffenorde's case<sup>7</sup>).

*Pain of Vagus and Cervical Origin Referred to a Region Supplied by the Fifth Nerve*—Whether the vagus, which sends sensory fibers to the posterior part of the ear and the cervicals, through communication with the carotid plexus, have sensory elements is still doubtful, but there is clinical evidence that vagal and possibly cervical plexus elements are among the causes of the continuation of the pain in some of the patients who continue to suffer after a complete resection of the sensory root of the trifacial nerve.

*Rôle of Peritubal and Supralabyrinthine Cells in Referred and Direct Facial Pains*—The peritubal cells are situated just below the surface of the petrous posterior to the suture between the petrous bone and the squama and the angle formed by the squama and the greater wing of

6 Fay, Temple. Observations and Results from Intracranial Section of the Glossopharyngeus and Vagus Nerves in Man, *J Neurol & Psychopath* 8 110, 1927.

7 Uffenorde W. Disturbances of the Trigemminus Originating in the Ear, *Munchen med Wchnschr* 73 2064, 1919-1920.

the sphenoid. They extend inwardly, posterior to the styloid foramen and anterior to the carotid canal.

There is thus formed a direct line of cellular tissue from the anterior part of the middle ear to the plane of the foramen spinosum<sup>8</sup> and these cellular elements, especially in pneumatic mastoid, are liable to congestion. In addition, there are at least four tracts of cells along the posterior-superior surface and under the curve of the superior semi-circular canal,<sup>9</sup> all of which tend to coalesce at the petrous apex.

*Characters of Referred and Spasmodic Pains*—Although the pain of suppurative disease confined to the external one third of the temporal bone may be referred to one or other regions of the tritacral nerve the pain is of quite a different character from the neuralgia of a true tic, the former is largely a headache associated with a peripheral or aching pain in the teeth or around the eye, while a true tritacral neuralgia is a sharp piercing spasmodic stab in the course of the nerve.

*Differential Characteristics Between the Referred Pain of Suppurative Lesions of the Bone and Ganglionic Disease Probably From a Filtrable Virus—Geniculate Ganglion Zoster*—Clinically there is reason to believe that true zoster is a disease of the sensory elements derived from the ganglionic crest which in lower vertebrates form the spinal ganglia, the sheath cells and the sympathetic as zoster attacks only the segmental sensory nerves.<sup>10</sup> The pain associated with the polyneuritis from nonsuppurative disease of the geniculate ganglion is referred externally to the ear and mastoid surface and is associated with herpes of the external auditory canal, the characteristics of the Ramsay Hunt syndrome.<sup>4</sup>

The pain which accompanies suppuration from geniculate ganglion involvement associated with congestion of the deep cells of the temporal bone is apt to be referred inwardly to the branches of the fifth nerve.

*Conclusions Concerning the Osseous Origin of Referred Facial Pain, in Cases with Recovery After Mastoid Operation*—(a) The facial pain in the majority of the benign cases is undoubtedly primarily of osseous origin, because as a rule it promptly disappears when the cellular cores of the mastoid and perilabyrinthine cells is removed. (b) The facial neuralgia is caused by a congestion of the peritubal and superior labyrinthine cells of the anterior surface of the petrous pyramid, either of which may extend to the region of the sensory communications of the facial and glossopharyngeal nerves as they lie on the superior sur-

<sup>8</sup> Girard L. Perilabyrinthine Cells. Soc. de laryngol. otol. et de rhinol. de Paris. Dec. 9 1911.

<sup>9</sup> Siebenmann Friedrich. Die Korrosions-Anatomie des Knochernen Labyrinths des menschlichen Ohres. Wiesbaden. F. Bergmann. 1890.

<sup>10</sup> Heard and Campbell. The Pathology of Herpes Zoster. Brain. 1900 vol. 23.



face of the petrous bone, communications of which pass beneath the gasserian ganglion (c) Irritation in this region may originate pain which is transmitted forward to one of the trifacial peripheral elements of the first, second or third branch (d) Pain of the geniculate ganglion from a filtrable virus—a polyncuritis—is transmitted externally to the drum membrane, external auditory canal or mastoid region

From an operative standpoint it may be stated that (1) a temporo-facial pain, or a neuralgic pain in the supra-orbital region around the eye or in the face or teeth, associated with or following an otitis, if unaccompanied by signs of sepsis cerebral irritation or labyrinthitis simply calls for the complete excitation of the mastoid cells with as much of their perilabyrinthine cellular elements as have direct communications which can be demonstrated macroscopically (2) This having been done the continuation of the facial pain only becomes of serious moment if the sepsis continues

(c) *Facial Pain from Direct Irritation of the First Branch*—When however, that portion of the floor of the middle fossa which is formed by the superior surface of the petrous internal to the eminentia arcuata is the seat of inflammation the trifacial nerve itself may be irritated

If the suppurative process (congestion or caries) involves the petrous apex, the resulting pain is apt to involve the first branch. Such a pain never occurs in suppuration confined to the posterior fossa

*The Significant "Pain Behind the Eye" in Suppurative Otitis*—Pain in the first branch limited to the region behind the eye is significant of irritation of the dura over the petrous apex, and in the presence of continued sepsis, signifies caries of the petrous apex

*Ophthalmic Branch a Spinal Nerve*—The ganglionic portion of the first branch of the fifth nerve is separate morphologically and developmentally from the rest of the nerve. The ophthalmic branch is in reality the highest dorsal spinal nerve as from an evolutionary standpoint the dorsal region of the body (controlled by the dorsal sensory roots) really ends at the tip of the nose. The area supplied by the ophthalmic branch becomes anatomically a ventral surface only in the primitive primates—*Prosimæ*<sup>11</sup>—by the anterior expansion of the neopallium. That the ophthalmic branch is in reality a spinal dorsal nerve is shown by its early appearance in the lower vertebrates as a separate nerve and by its connection with the spinal descending root which is present long before the appearance of the principal nucleus of the fifth nerve, the latter not being present in fishes, Brouwer<sup>11</sup> was unable to find any evidence of it

<sup>11</sup> Brouwer, B. Die biologische Bedeutung der Dermatomerie. *Folia Neurobiologica*, in Woollard. Recent Advances in Anatomy, Philadelphia, P. Blakiston's Son & Company, 1915, vol. 9, pp. 272 and 273

The principal nucleus of the fifth is first seen in *Amphibia* lying dorsolateral to the motor nucleus. Therefore in the fish all cutaneous fibers which enter from the head region must run in the descending spinal tract of the fifth nerve. In the selachians, *Dipnoi* and a few of the aquatic amphibians, the ophthalmic branch is separate<sup>12</sup>. Later it becomes joined with the supramaxillary and intramaxillary.

Clinically, the posterior sensory root nature of the ophthalmic branch is shown by the area supplied by it being the frequent seat of true zoster—which but rarely attacks other than the segmental portions of the neurospinal axis.

*Anatomic Peculiarities of Ophthalmic Branch*—In man the ophthalmic branch has a much longer course in Meckel's cave than the second or third branches. It is firmly adherent to the dura of the cave on its under and inner side, and to the cavernous sinus, from both of which it can be separated only with difficulty. Its ganglionic portion lies flat on the dura which is adherent to the bone of the petrous apex and the petrosphenoid articulation mesial to the sector supplying the second and the larger portion going into the third branch. It is slightly above the latter.

On the other hand, the ganglionic fibers of the second and third branches lie on the elastic cushion formed by the internal carotid artery as it runs in the open foramen of the carotid canal. Both the second and third branches enter the cave without adhesion to its dural covering. They also leave the cave anterior to the cancellous tissue of the petrous apex.

Anatomically, then, the ganglionic and peripheral portions of the second and third divisions of the fifth nerve are protected from osseous or dural inflammation, either of which may cause irritation of the ophthalmic portion.

*Susceptibility of Ophthalmic Branch to Dural Pulling from Swelling of Bone by an Underlying Suppuration*—Anatomically the first branch is especially apt to be affected by periosteal swelling as the fibers to the first branch pass over the cellular area of the petrous apex at its junction with the sphenoidal base, where cancellous tissue is apt to be abundant.

But probably it is the "pulling" in the area of its adhesion to the first branch the result of inflammation of the cancellous tip and petrosphenoid articulation that gives rise to the extra-ocular pain in the early stages of caries of the petrous apex as it is doubtful if inflammatory infiltration of the root alone—as occurs in the later stage of abscess formation—will originate pains.

<sup>12</sup> Wilder H. H. History of the Human Body. New York, Henry Holt & Company, 1923, p. 502.

In Turner's<sup>13</sup> case of sphenoid inflammation with cavernous sinus thrombophlebitis, the patient had no pain behind the eye, although a microscopic inflammatory infiltration of the ophthalmic nerve was demonstrated post mortem. I have had personal experiences of abscess infiltration from thrombophlebitis of the gasserian ganglion without fifth nerve pain.<sup>14</sup>

The freedom from pain in the domain of the third and second branches in petrous apex suppuration is probably due to the fact that they are not subject to dural pulling as they have no dural connection and are in relation with the compact tissue having no cellular elements which form the superior border of the petrous behind and of the carotid artery in front. This type of bone is not apt to transmit inflammatory swelling.

For even in extensive caries involving both the anterior and posterior surfaces of the petrous apex, the compact bone of the superior border remains unaffected (as in cases 1 and 2 of this series), in which case even with extensive destruction of the posterior wall of the petrous apex and a localized meningitis of the bulbous cisterna—associated with stiff neck, nystagmus, sixth nerve palsy with sepsis—there is no facial pain unless the middle fossa is involved by the carious process.

That the characteristic retro-orbital neuralgia is of dura-osseous origin and is not a true neuritis is shown by the fact that in non-suppurative lesions, true trifacial neuralgia—spasmodic tic douloureux—the pain always is spasmodically stabbing—neuralgic—in character and begins either in the second or third branch but never in the first, although the facial neuralgia involves the first branch at a later date. Again the pain in the supra-orbital or nasal nerves in tic douloureux is never retro-ocular, while the pain of suppurative disease of the petrous apex is cephalalgic (headache)—with a retro-orbital element.

*Conclusion*—Consequently, on anatomic grounds and from clinical experience, pain behind the eye may be the first manifestation of congestion or granulation caries of the petrous apex.

(d) *Facial Pains in Localized Meningitis*—If an extradural abscess forms during an infective osteitis, then a neuralgia from direct pressure of any branch of the trifacial nerve may occur (Gradenigo). Such direct pressure is doubtless the cause of the second and third branch pain in cases of exudate into the subdural space of the middle fossa. I have seen one case in which toothache was the result of a brain

<sup>13</sup> Turner and Reynolds. Nasal Mucous Polyp, Intranasal Operation on the Ethmoidal Air Cells, Purulent Meningitis, *J. Laryng & Otol* 41 717 (Nov.) 1926.

<sup>14</sup> Eagleton, W. P. Cavernous Sinus Thrombophlebitis, New York, The Macmillan Company, 1926, case 24, p. 153.

abscess another of cavernous sinus suppuration<sup>15</sup> and several cases of retro-ocular pain on filling the brain abscess with water<sup>16</sup> the pathologic lesion being confirmed by autopsy or operation

Also, I have seen numerous cases of localized meningitis of the base of the middle trossa secondary to bony caries of the external third of the petrous bone which have occasioned headache and pain around the eye, probably from a localized collection of fluid in the middle trossa, as the evacuation of the fluid associated with removal of the carious bone gave immediate relief to the pain

Value of Lumbar Puncture in Diagnosis and Treatment Clinically, localized meningitis may be eliminated by the absence of sepsis and an examination of the fluid obtained by lumbar or occipito-atloid puncture Consequently, it has become my practice before operation on the mastoid to perform lumbar puncture in all cases of facial pain as the absence of increased pressure and heightened cell count of the fluid adds security to the diagnosis of a nonfatal form of neuralgia

#### CLINICAL CONCLUSIONS ON TYPES OF SENSORY NERVE DISTURBANCE ORIGINATING IN OR NEAR THE SUPERIOR SURFACE OF THE PETROUS PYRAMID

There are four distinct types of sensory nerve disturbances which originate in or near the superior surface of the petrous pyramid all of which are clinically diagnosable during the early stages (*a*) referred pain from suppurative diseases of the ear, the pain originating from involvement of the communicating fibers of the facial, glossopharyngeal vagus, and possibly the cervical nerves, and referred to one or other branches of the fifth nerve, evacuation of the mastoid and adjacent cells only is indicated, (*b*) zona—from geniculate ganglion (sympathetic or spinal nerve) involvement—probably from a filtrable virus a hemorrhagic process associated with herpes, (*c*) true tic douloureux of unknown origin, and (*d*) first branch retro-ocular pain from caries of the petrous apex

The latter calls for an operative attack on the diseased area

#### II ABDUCTOR PARALYSIS DIAGNOSTIC SIGNIFICANCE

Dissection on cadavers would demonstrate that sixth nerve paralysis signifies either (1) periosteo-aponeuro-dural swelling in the posterior trossa when it accompanies suppurative disease of the posterior surface

<sup>15</sup> Eagleton (footnote 14 case 18)

<sup>16</sup> Eagleton Wells P. Brain Abscess Its Surgical Pathology and Operative Treatment New York The Macmillan Company 1922 case 13 pp 63 and 183

of the petrous or sphenoid or (2) cerebrial displacement in a brain tumor. The suppurative otitic lesions in their earlier stages are extracerebral, whereas a neoplastic process is entirely intracerebral.

#### ABDUCTOR PARALYSIS FROM DISEASE OF PONS, PERIOSTEUM, APONEUROSIS OR DURA

*The Development of Dorello's Canal*—The tissues forming Dorello's canal and Gruber's ligament—viz, (a) the periosteum of the bone of the apex of the petrous pyramid and the occipitosphenoidal base, with (b) the dural covering and (c) the aponeurosis of the petro-occipital articulation and the petrosphenoidal ligament uniting them—are developmentally one structure, inseparable from one another. They are all of mesoblastic origin, all modifications of fibrous tissue and all have one purpose viz, the protection of the central nervous system from injury by trauma or infection. It is the intimate relationship with the mesoblastic tissue surrounding the sixth nerve which makes it especially liable to pressure in inflammation of the periosteum, dura or aponeurosis.

*Resemblance Between Sixth and Seventh Nerves*—Anatomically, the sixth nerve has many points of similarity to the seventh—also a motor nerve. Like the facial nerve it is also frequently paralyzed in local suppurative disease and in fractures of the cranial base.

The sixth nerve as it leaves the pontile cisterna and enters Dorello's canal immediately loses its arachnoid covering, as does the facial nerve on entering the fallopian canal. The fifth nerve, on the other hand (largely sensory), has a free passage through a large tentorial ring, is surrounded by loose arachnoid prolongations and is bathed in cerebrospinal fluid.

Neither the facial nor the sixth nerve has a neural sheath from the time of its entrance into the respective canals until the exit—at the styloid mastoid foramen<sup>17</sup> and from the cavernous sinus, respectively.

Consequently, any pressure, be it inflammatory or traumatic, of the tissue forming the canals of the sixth and seventh nerves (aponeurodural in the case of the sixth, bony in the facial) will paralyze either the abductor or the facial nerve.

*Sixth Nerve Paralysis That Disappears After Mastoid Operation*—(See appendix.) My dissections in Paris established the bizarre character of Dorello's canal as regards its position, size, shape and anatomic formation as would necessarily result from the nature of its development, its position, size, shape and structure being determined by the configuration and symmetry of the bony base—a very irregular and

<sup>17</sup> Ballance, Charles and Colledge, L. Anatomic Observations of Nerve of Face and Neck. J. Laryng & Otol. 42:1 (Jan) 1927.

asymmetrical body. Consequently, the canal does not conform to any standard of length, diameter or circumference of lumen.

Even the nerve itself presents variations very unusual in the nervous system as it is frequently double with great variations in size or length.

#### ANATOMIC FACTORS INFLUENCING THE LIABILITY TO ABDUCTOR PARALYSIS IN DIFFERENT PATIENTS

Among the anatomic factors influencing the liability of different patients to abductor paralysis are

(a) The differences in the length of the nerve in the dural canal varying greatly as it does (see table)

(b) Its anatomic position on the bony basis (whether on the bone or on the articulating surface of the petrobasilar suture)

(c) The extent of the closure of the articulation between the petrous apex and the occipital and sphenoidal base which is among the last of the cranial sutures to undergo complete ossification, consequently the younger the patient the more extensive the aponeurotic fibers and the greater liability to transmission of dural inflammation by septic swelling. This may partially explain the greater frequency of abductor paralysis during the early decades.

(d) The closeness of its attachment to the periosteum. In this respect the sixth nerve is even more liable to paralysis than the facial nerve, as there are no fibrous connections between the bone and the facial nerve, which can be easily lifted out from its canal up to the point of its exit from the stylomastoid foramen while the sixth nerve in its whole course through Dorello's canal is united either tightly, or loosely by connective tissue fibers with the periosteum, the aponeurosis, Gruber's ligament or the dural covering.

(e) The great variation of the size of the nerve and its freedom in the canal. At times the nerve is tightly constricted and immobilized by the dura and the periosteum—as is the facial by the bone—and again it is moderately loose, allowing of considerable motion when pulled upon.

All the foregoing factors may influence the liability to abductor paralysis not only of the homolateral but of the contralateral side.

Thus swelling of any of the surrounding dura or aponeurosis may furnish pressure enough to paralyze the nerve even without inflammatory change in the bone itself. The latter is the direct paralyzing factor in the majority of the cases as well as the underlying cause in all. Thus with a long dural course and a closely attached canal slight inflammation of the periosteum or dura would cause paralysis of the sixth nerve. It is conceivable that a rheumatic toxic swelling of the

fibrous bands (tendinitis) of the articulation could cause sufficient pressure to paralyze a tightly held nerve

#### PARALYSIS FROM NEURITIS OF NERVE ITSELF

Pathologic evidence suggests that the sixth nerve only undergoes degenerative neuritis from pressure of the surrounding structures and is not paralyzed by changes of temperature as occurs in the facial nerve, the sixth being a pure motor nerve while the facial in the lower vertebrate is a mixed motor and sensory nerve and even in man contains sensory fibers, and thus is probably susceptible to the stimulus of changes in temperatures. Toxic agents such as diphtheria are frequently the cause of an abductor paralysis, the result of a peripheral neuritis

*Relation with Inferior Petrosal and Its Communications*—In its ascent on the posterior surface of the bone or on the articulation, the sixth nerve may be in relation with the plexus of veins emptying into the inferior petrosal sinus

#### OSSEOUS FACTORS IN THE PRODUCTION OF ABDUCTOR PARALYSIS

It is the character of the bone itself that decides whether the nerve will be paralyzed or not, depending on whether the bone structure is adapted to the transmission from a distance of congesting swelling, viz., whether or not the osseous structure of the petrous apex has an underlying cellular or spongy structure. A pneumatic bony structure with cells extending from the middle ear to the petrous apex is especially liable to the development of abductor paralysis. These are the cases in which recovery results after simple opening of the mastoid. The nature of the osseous structure is of special importance in those cases in which the nerve passes under the petrous spine. Here one of the abducens nerves may be almost completely surrounded by cellular bone, while that of the opposite side is entirely free of bony contact, as occurred in one cadaver. In such a case it is conceivable that slight swelling of the periosteum, sufficient to paralyze the abductor of the side contralateral to the suppurating ear, might be transmitted across the base to the contralateral nerve while that of its fellow may escape. This may be the explanation for some of the cases of contralateral abduction paralysis that have disappeared after a simple mastoid operation.

At the superior border of the petrous the sixth nerve may be subject to pressure from the petrosphenoid (Gruber's) ligament which, like all the other mesoblastic structures of this region varies greatly, as Gruber's ligament is only a part of the aponeurotic fibers uniting the

petrous with the mesial base. The direction of the fibers composing the ligament—from vertical to horizontal—dictates the size of the underlying canal, which may vary from a large canal in which the nerve lies free to a very small canal sending attachments to the nerve or even dividing the nerve into two portions.

#### RELATION OF ABDUCENS TO THE SPHENOID

Internal to the spine of the petrous apex, the sixth nerve may come in intimate relationship with the sphenoidal sinus, and when the sphenoidal body is diploic the nerve may be separated from the mucous membrane of the sinus simply by a thin layer of compact bone. This applies not only to the sinus of the homolateral, but occasionally to that of the contralateral side. This occurred in one cadaver in which an edematous swelling of the mucous membrane of the right sphenoidal sinus might have caused an opposite (left) abductor paralysis, as a posterior prolongation from the right sphenoid passed behind the left sinus and extended to the opposite petrous spine.

#### RELATION WITH VEINS OF PERITUBAL REGION AND ABDUCTOR PARALYSIS OF VENOUS ORIGIN

The abducens come into relationship with the plexus of veins which run from the anterior part of the inner wall of the tympanic cavity, through the bone of the petrous pyramid—peritubal region—to the cells of the petrous apex (Pietratori). A microscopic thrombophlebitis of these veins in the presence of a cellular bony apex might give rise to abducens paralysis.

#### ABDUCTOR PARALYSIS FROM INTERMENINGEAL SUPPURATION

In the early stages of a suppurative otitis it is the intradural or periosteal inflammation which causes abductor paralysis. However, when the pontile cisterna is the seat of an adhesive exudate from localized or general suppurative bulbar meningitis, the nerve may be paralyzed from the arachnoid inflammation itself.

I have seen an abductor paralysis associated with a low grade of papilledema which disappeared on evacuating an excess of cerebrospinal fluid by a lumbar puncture (M. L. case <sup>18</sup>). Contrary to the

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18 M. L. Case Report—Following mastoid operation a boy had pain behind the ears and eyes, he developed external homolateral rectus paralysis and a papilledema. Lumbar puncture showed apparently clear fluid, increased pressure, cell count 7, coagulable albumin a trace, of chlorides 0.71 and no micro-organisms. Second lumbar puncture a few days later showed clear fluid, still slightly increased pressure, increased trace of coagulable albumin, cell count 5, lymphocytes, chlorides 0.16 and no increase in globulin. Following this puncture there was a rapid subsidence of the papilledema.



generally accepted view, abductor paralysis is rarely the result of leptomeningeal inflammation—except as a terminal process—as shown by its absence in three of the four cases of bulbar meningitis, in all of which suppurative meningitis must have surrounded the nerve for a considerable period as demonstrated by autopsy. In the one case in which abductor paralysis was present it was manifestly a terminal process.

Anatomically, the liability to paralysis from suppurative intra-archnoid inflammation—localized or general suppurative or serous meningitis—is dictated by the (*a*) length of the nerve on the anterior surface of the pons (in the pontile cisterna) and (*b*) by the position, axis and size of the entrance of Dorello's canal, all of which conditions vary greatly in different cadavers, and on the two sides in the same cadaver. There is a small group of cases in which lumbar puncture causes a prompt disappearance of the symptoms, the lesion apparently being a nerve congestion from irritation of an overlying infective otitis.<sup>18</sup>

### III LOCALIZED BULBAR CISTERNA PONTILE MENINGITIS

#### ANATOMIC PORTION

As clinical experience has taught that (1) the site of the primary focus of osteitis or phlebitis determines where the infection enters the arachnoid, and as postmortem examinations have demonstrated that (2) the course which the meningeal inflammation takes after passing the dura is largely dictated by the normal channels in the arachnoid meshes with their connections into the cisterna (similar, to a certain extent, to the course that a phlebitis must take in a large venous sinus following its lumen and connections), and as there is postmortem and clinical evidence that in all types of meningitis nature makes an effort to limit the disease, it would appear reasonable to assume that if a diagnosis can be made of the exact site of the infection while it is limited to a particular area—be it the cisterna of the angle or of the bulb—cure from surgery should be obtained in a considerable proportion of cases of meningitis, as in cases of empyema of the ductus endolymphaticus and of the internal auditory meatus. Consequently, an effort was made to ascertain the direction in which otitic suppurative meningitis should advance in the meshes of the arachnoid of the posterior fossa, if such advance is dictated by the anatomic formation of the spaces.

A succession of cadaver "heads" arterially injected were dissected in which a dye had been allowed to diffuse (*a*) from the labyrinth into the subarachnoid spaces surrounding the internal auditory meatus and (*b*) from the region of the jugular bulb, two areas, which when attacked by suppurative disease frequently give rise to meningitis.

## EXPERIMENTAL PORTION

For surgical reasons the posterior fossa may be divided into an anterior and a posterior compartment. The line of division is the arachnoid prolongation surrounding the nerves leaving the brain.

Anatomically there can be distinguished the following sites, from which a carious process of the posterior surface of the petrous bone may cause a localized meningitis of the posterior fossa by extension through an arachnoid prolongation: (*a*) in the region of the ductus endolymphaticus, (*b*) through the prolongation surrounding the internal auditory meatus, (*c*) in the cisterna of the angle, and (*d*) of the bulbar cisterna (*e*) by way of an unnamed prolongation to the superior border of the petrous internal to and above the internal auditory meatus (possibly the arachnoid surrounding the remains of the structure entering the fossa subarcuata and (*f*) by way of the region through which the ninth, tenth and eleventh nerves pass out of the anterior compartment of the jugular fossa.

The diffusion by gravity of dye when placed in the meshes of the arachnoid connected with the labyrinth and the lateral sinus—both the frequent cause of septic leptomeningitis—furnishes (1) a graphic map of the region that infection will take as dictated by the anatomy of the arachnoid pathway, and (2) the points at which the infection can easily be limited by adhesions.

Dye in solution placed in an arachnoid prolongation after passing into a cisterna, diffuses into the other prolongations of the cisterna, but the communication of the arachnoid prolongation pathways of the posterior fossa from the cisterna are so small that particles of dye in suspension may be prevented from reaching the cisterna in many localities although dye in solution passes freely. This shows the ease with which different areas of arachnoid may be walled off, and infection thus limited by inflammatory reaction.

1. Dye introduced into the arachnoid prolongation surrounding the internal auditory meatus has a tendency to go (*a*) forward and upward into the middle fossa by way of the third nerve region, (*b*) around the superior collar of the cerebellum and (*c*) downward along the anterior surface of the medulla and cord without entering, to any great extent the pontile cisterna itself. This latter area is apparently protected by (1) the close mesh of the arachnoid, (2) the latter's adhesions to the basilar artery and (3) the arachnoid's flat position on the bony base.

2. Dye placed around the jugular bulb has a tendency to diffuse backward under the cerebellum and down the posterior surface of the cord—the posterior compartment.

3. Dorello's canal surrounding the sixth nerve does not admit any dye.

4 Dye in the prolongation of the fifth nerve extends halfway across the floor of the middle fossa

#### SYNOPSIS ON CLINICAL PORTION

Two cases of caries of the petrous apex from suppurative otitis are reported, both presenting the suggestive "pain behind the eye," associated with a low grade of chronic sepsis and recurrent attacks of slightly stiff neck

In one case these prodromal signs lasted sixteen days and in the other forty-three days before the onset of symptoms of bulbar cisterna meningitis. The symptoms of bulbar cisterna meningitis I believe are pathognomonic, viz. (a) semiconia from which the patient can easily be aroused, (b) supine position of the patient (on back) with the eyes closed and (c) intermittent recurrences of vertical nystagmus

All signs of posterior fossa involvement so usual in severe headache, great restlessness and opisthotonos but unaccompanied by cortical meningitis, were associated with a high fever and rapid pulse. Repeated trials of visual fields revealed great bilateral variations and the sudden appearance of a bitemporal hemianopsia somewhat resembling pituitary tumor pressure

The fluid from the lumbar region was cloudy, but contained no organisms. Autopsy in both cases disclosed a large carious cavity involving the petrous apex and extending onto the anterior and posterior surfaces of the petrous pyramid, causing a localized meningitis of the pontile cisterna followed by a general suppurative meningitis as a terminal process

The anatomic location of the focus of suppuration explained the clinical symptoms of fifth nerve pain and bulbar cisterna infection—a combination of middle and posterior fossa symptoms with extension into the chiasmal cisterna

Two additional cases of bulbar meningitis of traumatic origin are also reported, a clinical diagnosis of bulbar meningitis having been made during life because both patients presented similar clinical pictures without primary middle fossa involvement

Autopsies confirmed the diagnosis that the meningeal process in the early stage was confined to the bulbar cisterna

#### REPORT OF CASES

*CASE 1—Pontile Cisterna Meningitis the Result of Caries of the Petrous Apex Which Also Produced Secondary Labyrinthitis*

*History*—J. McE., 37 years, on March 5, following an attack of influenza, had a right-sided earache followed by a profuse discharge which continued until March 15, when the otorrhea lessened. During this time he had a slight rise in

temperature, complained of headache pain behind the eye and severe pain in the right side of the face and jaw extending back to the right ear all of which he attributed to neuralgia

March 16 Dr J J Mann found a moderate discharge from the ear with a slight drooping of the posterior-superior wall and a little tenderness over the antrum. The temperature was 102 F. A roentgenogram showed that the antrum alone was involved. The next day the symptoms had improved, but the tenderness had lessened. During the following ten days the patient did not return to Dr Mann, as he continued to improve although at times he had 'neuralgia' pains in and over his eyes and in his temple.

March 28 After passing several restless nights he suddenly developed a facial paralysis on the right side and total deafness in his right ear associated with spontaneous nystagmus and unsteadiness of gait. He was sent by Dr Mann to the Newark Eye and Ear Infirmary. The chief complaint was facial paralysis followed by pain in the right eye for the previous ten or twelve days.

*Examination*—The patient was right-handed. He did not look sick but had the whitish appearance of chronic nephritis. There was a slight aural discharge, with right-sided facial paralysis and deafness and spontaneous nystagmus to the left (away from the suppurating ear).

The right pupil was smaller than the left, which was explained by the patient who said that the vision of the right eye had never been as good as the left. The right cornea was sensitive, but apparently less so than the left. The disk margins of the right eye were blurred, and the vessels were engorged. The visual field suggested a bitemporal indentation. The temperature was 99 F and the pulse rate 80.

On lumbar puncture the fluid was not under pressure, and was clear (5 cells per cubic millimeter), it contained a trace of albumin, the globulin was not increased, the sugar reduction was normal, and the chloride content was 0.67. Urinalysis revealed, specific gravity, 0.20, albumin, 1 plus granular casts, 3 plus, squamous epithelium, 1 plus, pus cells, 3 plus, red blood cells, 2 plus. The blood pressure was 140.

*Diagnosis*—"Acute labyrinthitis with involvement of the horizontal semicircular canal from subacute otitis media."

It was decided (chiefly because the negative cerebrospinal fluid changes apparently denoted an absence of meningeal involvement) to allow time for the labyrinthine lesion to become fully localized.

March 29 to 30 The patient apparently was in excellent condition. Nystagmus was lessened. There was no pain in the head, but once during the night he felt pain in the right eye (to which proper attention was still not paid). The temperature varied from 98.3 to 99.4 F, the pulse rate, from 72 to 88.

March 30 The patient passed a bad night. He complained of severe pain over the right eye, and his temperature reached 101 F. The following morning however, the temperature was 100 F and the pulse rate 80 and the pain in the eye had lessened considerably. Slight rigidity of the neck was now noted for the first time.

*Reoperative Diagnosis*—"Acute non-suppurative labyrinthitis with a probable erosion of the external semicircular canal associated with a localized meningitis the result of congestion of the cells under the triacial, the latter probably secondary to invasion of the perilabyrinthine cells."

*Comment*—The mistake was made of not appreciating that an acute labyrinthitis which had followed a period of retro-ocular pain was at least suggestive

of infection of the labyrinth secondary to suppuration of the apex of the petrous, rather than extension from the antrum

*Operation*—The mastoid was opened. pus and granulation were found in the cells and antrum. The external arm of the horizontal canal was eroded and replaced by granulation tissue. The solid angle was removed, as well as the cells behind and above the horizontal canal. The posterior semicircular canal was exposed, just behind which, from the region of the ductus endolymphaticus, a drop of pus was evacuated. A small opening in the dura of this region liberated a considerable quantity of cerebrospinal fluid from which *Streptococcus non hemolyticus* was cultivated.

*Comment*—I did not explore the gasserian ganglion region of the middle fossa because in a rather large experience of cases with irritation of the branches of the fifth, evacuation of the cerebrospinal fluid from the middle fossa had been followed by relief. Not sufficient attention was paid to the persistence of localized pain behind the eye, in the face and temple, suggesting, as it did, a definite lesion of the petrous apex. But as the operative observations were felt to warrant the preoperative diagnosis, I expected the man to recover, although one of my associates called attention to the presence of the nystagmus, which was now toward the side of the lesion, as suggestive of a brain stem involvement.

*Postoperative Course*—The patient had no more than the usual postoperative discomfort during the first night, he slept irregularly. The temperature was around 101 F. On the following day (April 1), however, his temperature became elevated and continued from 103.3 to 104.4 F., he suffered from incontinence and had a stiff neck, he developed a peculiar type of stupor, that is, although he lay continuously flat on his back with his eyes closed and head retracted on being spoken to he would immediately open his eyes and promptly answer questions, stating that he did not feel "so good."

The patient now, although manifestly suffering from meningitis—as in addition to the stiff neck he had an internal strabismus—(from complete paralysis of the right external rectus) and a vertical nystagmus, there was an entire absence of the usual meningeal restlessness, headache and screaming.

The intra-ocular tension was very low in both eyes (10 mm. of mercury, Schiotz), which probably was due to the loss of cerebrospinal fluid on the previous day.

A second lumbar puncture revealed turbid fluid, with a white cell count of 4,000, a red cell count of 1,200, globulin and no micro-organisms.

*Diagnosis*—A diagnosis was made of acute fulminating suppurative meningitis of the lateral prolongation of the pontile cisterna from extension through the modiolus, secondary to suppurative labyrinthitis.

*NOTE.* The vertical nystagmus was explained by the supposition of an injury to the cerebellum associated with the previous operation.

*Second Operation*—With the patient under local anesthesia the common carotid was ligated without occasioning any circulatory disturbance. The vestibule of the labyrinth was opened from behind by throwing the posterior arm of the horizontal canal and the posterior vertical semicircular canal together. There was no pus in the vestibule but possibly a little blood. The cochlea was opened from the middle ear through the promontory but was found empty. The arachnoid prolongation surrounding the internal auditory meatus was incised from behind the pyramid and a large quantity of cerebrospinal fluid evacuated. The middle fossa was not opened because of the outstanding posterior fossa symptoms, viz., vertical nystagmus, sixth nerve paralysis, stiff neck and retraction of head completely filled the clinical picture.

*Subsequent History*—April 2 The patient continued to be in a semicomatose state with continuously high temperature and rapid pulse, but could be easily aroused. He gave the impression of being in nephritic coma as he had little of the restlessness or the crying out of meningitis. There was lateral deviation of the eyes to the right and upward. The vertical nystagmus disappeared but recurred on the following day. Lumbar puncture now revealed streptococci.

*After-Treatment*—Repeated lumbar punctures were made associated with blood transfusions.

April 4 The patient died of terminal pneumonia.

*Postmortem Examination*—The petrous apex was the seat of a carious process which had eroded both the anterior and posterior surfaces of the pyramid, but with the compact bone of the superior border of the petrous tip still remaining. The area of caries was about two thirds of an inch long and one third of an inch wide on the floor of the middle fossa, and slightly smaller on the anterior wall of the posterior fossa. The cavity in the bone was much deeper than appeared externally; the cavity undermined the internal auditory meatus extending below and anterior to it. Mesially, the carious process reached the petroso-occipito-sphenoidal suture. The bony cavity was filled with granulation tissue and pus. On the anterior surface the granulations were compressed and held flat by the dura covering it. It gave the usual appearance of granulation tissue which had been held under pressure for some time. On the anterior surface of the petrous the root of the gasserian ganglion was involved, the ganglion itself being edematous. The outer surface of the dura covering the gasserian ganglion was hemorrhagic.

On the posterior surface of the petrous the granulation tissue spread beyond the level of the bone and was here covered with pus.

*Meninges* There was practically no meningitis of the cortex, but a little meningitis confined to the bulbar cisterna (over the pons and medulla as it lies on the occipital process below the posterior clinoid process).

*Brain* The basal ganglion (optic thalamus) of both sides appeared blackened and degenerated as if containing multiple hemorrhages. There was no internal hydrocephalus but moderate distention of the third ventricle.

*CASE 2—Localized Caries of Apex of Petrous Pyramid Without Labyrinthitis the Route of Invasion Having Been Through the Supratubal Cells and Associated with a Chronic Meningitis of the Bulbar Cisterna the Latter Existing for a Considerable Period Before Becoming General*

*History*—A. R., a young woman had acute right-sided otitis five years before examination. On Dec 8 1926, she had pain in the right side of the head and a discharge from the right ear accompanied by vomiting.

December 18 She was admitted to the Newark Eye and Ear Infirmary on the service of Dr John Hemsath, with a diagnosis of acute right-sided mastoiditis. The temperature varied from 99.3 to 101.1 F.

December 20 A simple mastoid operation was performed. Pus and granulations were found in antrum and mastoid cells. A culture from a smear from the mastoid showed *Streptococcus nonhemolyticus*. The patient was discharged six days later apparently in excellent condition.

Jan 4 1927 She was readmitted to hospital complaining of irregular pain in the head and general malaise with profuse discharge from the mastoid wound and ear. The temperature and pulse were normal. She remained in the hospital until January 28 during which time she had several attacks of rather severe pain in the head which were relieved by dressing of the wound. On January 13 she

complained of slight dizziness, in addition to the headache. The former disappeared and did not return, but the headaches persisted irregularly, at times being almost entirely absent and again severe. The temperature varied between 98.3 and 100.3 F, but on one occasion it reached 101 F, and on another 102 F. The visual fields were suggestive of bitemporal hemianopic contraction.

January 14. The patient complained of a stiff neck accompanying her headache. The visual field was suggestive of right-sided hemianopic indentation. A few days later (January 18) the visual field was suggestive of left-sided hemianopic indentation.

January 22. The patient cried with a severe pain on the right side of her face.

Repeated blood counts showed erythrocytes, 4,800,000, hemoglobin, 85 per cent, leukocytes, from 9,200 to 8,400, polymorphonuclears, 78 to 80 per cent, lymphocytes, from 20 to 22 per cent. Cultures were negative. The Wassermann reaction was negative.

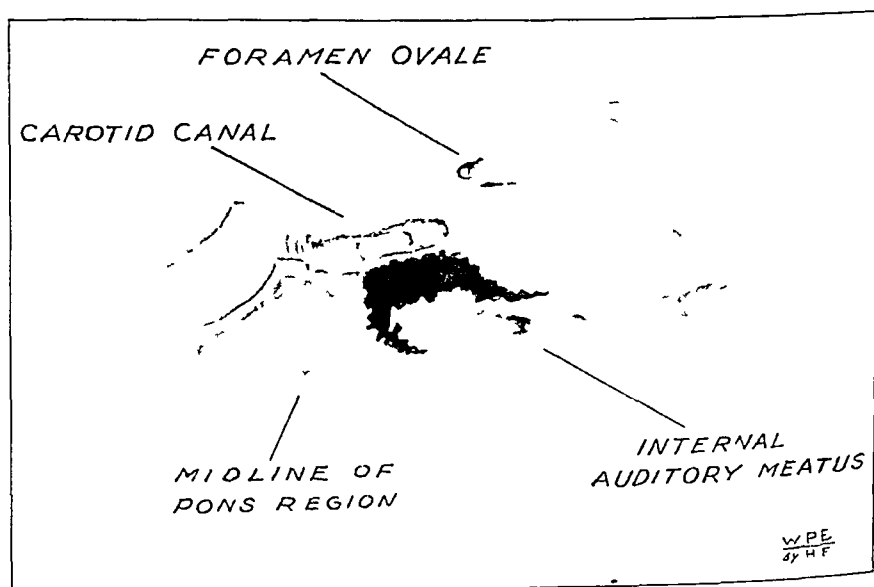


Fig 1 (case 1)—Caries of the petrous apex showing erosion on the superior surface.

February 8. The patient had considerable pain over the right eye, the pain in the head now being definitely located in this region. She also had severe dizziness and pain in the back of the neck. The temperature varied from 99 to 102 F. The visual fields were suggestive of a bitemporal hemianopic indentation.

February 18. The patient was transferred to the Cranial Surgery Department with the statement that "during the past ten days the patient has had attacks of pain in the head and over the right eye, a slight stiff neck, and an irregular temperature, 100 to 101 F, and that on the previous night she had had an attack of severe dizziness, associated with nystagmus and vomiting."

The temperature suddenly rose to 106 F, and the pulse rate to 120. The patient was now complaining of severe pain in the left side of the head. The neck was markedly stiff.

*Examination*—There was spontaneous horizontal nystagmus to the right, with a tendency to divergence. The disk margins of the right eye were slightly indistinct.

unct the vessels were full tortuous and dark. Hearing on the affected side was present but reduced. There was weakness of the left lower side of the face (opposite to the side of the suppurating ear). The tongue protruded in the midline. All reflexes were diminished. The blood count showed leukocytes 16,000, polymorphonuclears, 86 per cent, lymphocytes, 14 per cent.

Lumbar puncture showed a pressure of 20 mm of mercury, cloudy fluid 3,500 cells per cubic millimeter, chiefly polymorphonuclear, coagulable albumin, slightly increased globulin, chloride content 0.63 and no micro-organisms.

Roentgen examination showed moderate cloudiness of the right frontal sinus and the right ethmoids.

The visual fields showed marked bitemporal contraction of both fields.

*Diagnostic Impression*—The diagnostic impression was right cerebellar abscess with secondary meningitis. Of course the fact that she had severe pain in her eye would make it look as if the middle lobe was affected, but the marked nystagmus puts the infection in the posterior fossa. It may be that she has a meningitis of the whole of the base causing the nystagmus.

*Third Operation*—The right common carotid was ligated. The solid angle was removed. The lateral arm of the right cisterna pontis opened and a large quantity of fluid evacuated. An explorative puncture of the cerebellum for abscess was negative. Puncture of temporal lobes also revealed negative results. In the performance of the puncture a distended right lateral ventricle was tapped.

Death resulted in coma from meningitis four days after operation.

The lumbar fluid remained sterile until the day prior to death, when it contained streptococci.

*Postmortem Examination*—On removal of the dura from the right petrous bone, the apex was seen to be the seat of a cavity. Into this cavity a probe could be passed the distance of two thirds of an inch. It involved both the anterior and the posterior surfaces of the petrous pyramid with the compact bone of the superior border of the petrous remaining. The cavity was filled with semisolid yellowish material, which looked like cholesteatoma. The mass was apparently held in shape by the overlying dura. On the anterior surface of the pyramid, the carious area lay under the fifth nerve the overlying ganglion being edematous and surrounded by granulation tissue. The purulent granulomatous mass included the carotid canal, although the carotid artery was pervious. The adjacent cavernous sinus was apparently obliterated, for its cavities could not be found; however, it did not contain pus. The posterior surface of the petrous apex was also eroded, the orifice of the cavity on this surface extended from the petro-spheno-occipital suture mesially to within one-third inch of the inner border of the internal auditory meatus, the latter in its depth was undermined by the carious cavity. The pathologic cavity was one-half inch in width, three-eighths inch in length and three-eighths inch in the vertical plane. It contained a mass of cheesy pus and detritus which resembled cholesteatoma.

*Comment*—The location of the cavity involving both the anterior surface of the petrous (that is the floor of the middle fossa) and the anterior wall of the bulbar depression in the posterior fossa, explained the combination of symptoms of gas-serian ganglion pain and marked nystagmus of bulbar origin.

*Postmortem Examination of Meninges*—From the boni locus there had originated a meningitis of the bulbar cisterna, which latter was the site of a purulent exudate. This exudate extended from the pontile region forward to the chiasmatic cisterna and laterally the process had broken loose from the bulbar



cisterna, where it had been confined for a considerable period, spreading, as it did, from the bulbar cisterna forward into the chiasm and laterally over the cerebellum.

The terminal diffuse meningitis was only a sequela of the localized meningitis of the bulbar cisterna.

The distinct limitation of the carious process is found post mortem warranted the belief that the case offered a good prospect for recovery had the condition been diagnosed early and radical operation been performed with drainage of the infected bony tract along the floor of the middle fossa. And even at a much later period (when the dizziness and stiff neck gave warning that the posterior fossa was affected), the localization of the meningitis to the bulbar cisterna, which had resulted from a slow localized caries, showed that the septic processes were still controllable if a radical attack on the carious area even then had been associated with evacuation of the fluid in the bulbar cisterna.

*Comment on Cases 1 and 2*—Both cases 1 and 2 contain distinct aspects of similarity which should have allowed an early diagnosis of (1) caries of the petrous tip, and later (2) of meningitis of the bulbar cisterna, the latter condition invariably resulting from the former when unrelieved by surgical intervention. As a result of these two pathologic processes both cases presented (3) a symptom complex of middle fossa and posterior fossa (bulbar cisterna) involvement, and this in chronologic order.

(1) Symptoms of Caries of the Petrous Apex (Middle Fossa Symptoms) Both patients had pain referred to the first branch of the trifacial nerve for a considerable period of time before meningitis became outstanding. In A. R., the pain lasted from January 22 to February 18 (twenty-six days), in J. MacE., from March 15 to April 1 (fifteen days).

The pain in the face and teeth probably was due to involvement by the carious process of branches to the sensory root, and of the dura, which is very adherent to the bone largely because of the passage of fibers of Arnold's nerve with the great superficial petrosal in the hiatus fallopii.

Dissection on cadavers has shown me that the nerve connection which passes under the gasserian ganglion cannot be separated easily from the bone, although extradural and on the surface of the bone itself.

The retro-ocular pain—pain behind the eye—was referable to an involvement by edema or inflammatory infiltration of the dura itself, with a pulling on the first branch, as in both cases. At postmortem examination, "the outer surface of the dura of the gasserian region was more or less hemorrhagic."

(2) Symptoms of Bulbar Cisterna Meningitis (Posterior Fossa Symptoms) (a) Both patients had early stiff neck associated with (b) subacute sepsis, viz., general malaise, headaches, restlessness at night and irregular slight temperature in the presence of an otitis. This slight stiff neck was the first manifestation of an involvement of the carious process into the bulbar cisterna of the posterior fossa. This meningeal lesion which, for a considerable period, remained localized ultimately presented a symptom-complex, which I believe to be diagnostic of bulbar cisterna meningitis.

(c) There was nystagmus of brain stem origin, viz., at first toward the side of the lesion and later vertical in direction, associated with (d) a stupor, which resembled the stupor of cerebellar abscess—accompanied by stiff neck—little headache, high temperature, high cell count of the sterile fluid from the lumbar region, but unassociated with the violent headache, restlessness and delirium of cortical meningitis.

This bulbar cisterna meningitis after remaining localized for a variable time spreads forward and may cause (1) a bitemporal contraction of the visual fields, which was present in both cases and may be of the greatest diagnostic importance

(3) Other Points of Similarity in the Two Cases Both cases showed a hemorrhagic process in the basal ganglion of the brain, concerning the origin and significance of this I have nothing to offer

Both cases showed absence of the sixth nerve involvement until the period of terminal meningitis

Neither case showed an internal hydrocephalus so frequently present in the usual cases of meningitis of the posterior part of the base

*CASE 3—Fracture of Cribriform Plate of Ethmoid and Pneumococcus Meningitis of the Bulbar Cisterna*

*History*—One week before examination a child fell, hitting his head against a stone and receiving a small cut on the right side of the nose. The wound became infected. The patient became feverish and restless. Three days later he began to have severe headache and stiff neck, followed by difficulty with speech and semi-consciousness. He was brought to the City Hospital on the seventh day after injury.

*Examination*—The patient lay quietly in a semicomatose condition, from which he could be aroused. He was irrational at times, however. The temperature was 104 F. The pulse rate was fast and variable. The frontal region showed a small hematoma (and a burn from the use of a strong liniment which had been applied to relieve his headache).

*Eyes*—There was a small laceration of the skin over the lacrimal region of the inner side of the right orbit, but no discharge. There was no ecchymosis of the lids or conjunctiva; the pupils were equal, and reacted to light and in accommodation, but had a spontaneous horizontal nystagmus which became vertical on looking upward. Hearing was present in both ears, there was no bleeding.

There was marked rigidity of the neck, which the father said had been present for three days. A marked Kernig sign was seen on the left side, it was slight on the right. The knee jerks were active. The Brudzinski sign was positive, the cremasteric reflex positive and the abdominal reflexes absent. A roentgenogram for fracture of the cribriform plate was negative.

On lumbar puncture the fluid was found under marked pressure, it was clear and contained but 392 cells per cubic millimeter and pneumococci (gram-positive diplococci).

*Diagnostic Impression*—The diagnostic impression was "From the horizontal and the vertical nystagmus (brain stem), the retracted position of the head, and especially from the fact that he has not the meningeal cry, but lies in a stupor from which he can be aroused, I am of the opinion that the patient has an involvement of the cisterna of the brain stem, that is, over the pons."

*Suggested Treatment*—Because of the similarity of the clinical picture to patients A. R. and MacE (cases 2 and 1) who had definite lesions in the bulbar cisterna, I removed the child to the Eye and Ear Infirmary with the idea of washing out the bulbar cisterna by the introduction of a cannula passed through the inner side of the orbit and then intradurally along the lateral wall of the cavernous sinus and continued through the subarachnoid prolongation of the fifth nerve, thus opening into the basal cisterna which latter at this point extends a considerable distance anterior to the plane of the pons. Although I had practiced this puncture on several cadavers (sometimes without puncturing the cav-

ernous and again entering either it or the middle fossa), when it came to performing it on a living patient I was reluctant to submit him to the risk.

*Treatment*—Occipito-atloid puncture was performed. The fluid at first was slightly bloody but soon became clear, it contained no cells but numerous pneumococci.

*Subsequent History*—The patient continued in unconscious state with occasional periods of restlessness, high temperature and rapid pulse.

Lumbar puncture showed fluid under pressure, it was cloudy, straw-colored and contained pneumococci.

*Postmortem Examination*—A small fracture was seen through the posterior portion of the cribriform plate. There was no hemorrhage into the orbit, but a small spot of ecchymosis into the brain cortex over the site of the fracture. The meninges of the base of the brain showed exudate in a typical ring surrounding the brain stem, which was distinctly marked and outlined by the limited exudate (fig. 2). The upper part of the cord was also surrounded by a thick exudate.

In addition to this exudate around the brain stem, there was a thick exudate in both the ventricles so that it could be readily wiped away. (Whether this shows that the infection was primary only in the ventricles and then passed into the brain stem, I do not know, but I think it was the other way about, viz, that it went from the brain stem into the ventricles.)

While there were a few spots of exudate in the cortex, nearly all were situated beside the longitudinal sinus, showing how nature was making an effort to eliminate the infection by carrying the exudate into the veins themselves, and that the venous congestion so usual in cases of meningitis is a protective process of nature.

The tract of cerebral injury did not seem to go into the ventricle, although there were also little spots of ecchymosis in the brain.

The convolutions were obliterated, showing that the internal hydrocephalus in these cases was probably due to ventricular exudate.

(At the completion of the postmortem examination, I passed a probe through the opening near the lacrimal sac backward, and entered the gasserian ganglion. I probably could have washed through the infected bulbar cisterna by means of one cannula introduced by this route and another cannula in the occipito-atloid region.)

*Comment*—It would seem from this case that the washing out of the base by Van Allen's method, and possibly the washing out of the ventricles (for the brain was under great tension) is feasible in certain cases.

*CASE 4—Bulbar Cisterna Meningitis. Infection Entering the Arachnoid from Below by Way of the Pharyngeal Plexus Following an Infected Wound of the Posterior Pharyngeal Wall and a Fracture of the Anterior Part of the Body of the Cervical Vertebrae.*

*History*—On September 30, the patient was shot, the bullet from a large revolver passing through the left molar region and driving a tooth in front of it which lodged in the mucous membrane of the soft palate. After traversing the base of the tongue, the bullet perforated the posterior pharyngeal wall and lodged in the soft tissues of the opposite side of the neck. On admission to the hospital, the patient was conscious, complained of pain on the right side of the neck which was somewhat swollen. He was expectorating considerable blood. A large lacerated wound of the palate, tongue and nasopharynx, made by the bullet, could be distinctly seen.

During the next few days the temperature varied from 100.4 to 102.3 F but on October 6 rose to 104.5 F. The stiff neck was thought to be due to the suppurating wound. The bullet discharged spontaneously into the nasopharynx.

The patient was fed by stomach tube and was given aseptic lavages to combat infection.

October 7. There was an high irregular temperature varying from 105 to 102 F accompanied by several chills and sweats. The blood cultures were negative. The leukocytosis was 18,600.



Fig. 2 (case 3)—Ringlike exudate in bulbar meningitis beginning in the pontile cisterna and extending around the hair stem.

October 11. The patient was restless but there was no headache or other sign of meningeal irritation.

October 13.—The temperature again reached 105 F, following a chill. There was no headache. The patient was slightly irrational and pulled the tube from his throat.

Within a few hours he presented the typical picture of bulbar cisterna meningitis. He lay on his back with the eyes closed but could be aroused, there was a slight stiff neck but no more than was present ever since injury. There was incontinence associated with a high temperature slight restlessness but no headache. Lumbar puncture revealed milky fluid not under pressure. The cell

count was 2,800, the globulin reaction was 3 plus, and micro-organisms were found, probably streptococci

The patient died twenty-four hours later

*Postmortem Examination* (Dr. Harrison S. Martland) —Postmortem examination revealed fracture of the anterior portion of the body of the third cervical vertebra, surrounding which was a sloughing infiltrated mass, a dissecting abscess between the bone and mucous membrane, with many thrombosed vessels. The fracture did not enter the spinal canal. The bone of the base of the skull was normal.

*Meninges* Purulent exudate filled the bulbar cisterna on the anterior surface of the pons, from which it extended under the inferior surface of the cerebellum, and followed the basilar artery upward into the region of the third nerve and into the chiasmal cisterna from which a little exudate ascended into the sylvian fissure. There was no exudate on the superior surface of the cerebellum. Opening of the venous sinuses disclosed a purulent clot on the region of the torcular Herophili.

The internal organs showed signs of general sepsis.

*Postmortem Comment* —The pus over the inferior surface of the cerebellum was apparently an overflow, the same as the slight amount of pus in the sylvian fissure. The infection must have entered the meninges through the pterygoid or pharyngeal plexus of veins.

The pus in the region of the torcular may have been secondary to the meningitis or simply a part of the general venous sepsis.

#### CONCLUSIONS

The abducens is the most primitive of the ocular motor nerves and is in intimate relationship with the mesoblastic tissues of the cranial base, consequently it is most frequently paralyzed by suppurative lesions, not, as is generally supposed, because of its long course. These intimate relationships do not vary greatly in different cadavers and on the two sides of the same cadaver.

Abducens paralysis of the homolateral or contralateral side, when associated with a suppurative lesion, should be considered as only a small part of the clinical picture in the localizing of the site of the lesion or the nature of the process.

The periosteal-aponeurotic dural nature of Dorello's canal and the peri-dura-arachnoid structure of the fifth nerve furnish a satisfactory anatomic explanation of the different clinical types of fifth nerve irritation and abductor paralysis in those cases in which recovery follows after mastoid extirpation. The evolutionary development of the first branch of the trifacial and its anatomic connectives furnishes a satisfactory explanation of the significant "pain behind the eye" in cases of the petrous apex.

In the differential diagnosis of the types of meningitis, a proper appreciation of (a) the various causes and forms of facial pain and (b) abductor paralysis and the recognition of the (c) syndrome of bulbar cisterna involvement must play an important part.

Both facial pain and abductor paralysis in suppurative diseases of the middle ear furnish valuable localizing information for the diagnosis between intradural and intra-arachnoid inflammation if the surgeon distinguishes between congestion and caries—and between intra-Dorello and intracranial involvement—as he diagnoses facial paralysis of central and peripheral origin.

Properly interpreted either facial pain or abductor paralysis will enable a localizing diagnosis of (a) caries of the apex of the petrous pyramid, (b) localized pontile cisterna meningitis as the result of such caries (c) suppuration of the sphenoidal sinus, and (d) thrombophlebitis of the cavernous sinus and associated petrosal and basilar veins all at a time when surgical intervention promises hope for recovery.

In the benign cases, temporotacial pain is a referred pain from irritation of a sensory communication from congestion of the bone in that portion of the anterior surface of the petrous pyramid where the geniculate ganglion superficial great petrosal and vidian branches of the glossopharyngeal nerve are given off, as in this region the nerves are in bony canals, are extradural, and cannot be separated from the bone. The osseous congestion or dural irritation originating the pain may be more or less quiescent, and still cause pain for a considerable period.<sup>19</sup>

Thus temporotacial pain or even a neuralgic pain in the supra-orbital region around the eye or in the face or teeth, associated with or following an otitis, if unaccompanied by signs of sepsis, cerebral irritation or labyrinthitis, simply calls for a complete removal of the mastoid cells with their perilabyrinthine cellular connections. This having been done, the continuation of the pain only becomes of serious moment whenever the sepsis continues.

First branch pain—pain behind the eye—in the presence of sepsis is significant of caries of the petrous apex from dural pulling of the middle fossa, and if unrevealed by mastoid examination or if associated with signs of posterior fossa irritation—bulbar meningitis irregular stiff neck, sixth nerve paralysis—it calls for the opening of the apex.

Symptoms of localized pontile meningitis originate from irritation of the cortex of the anterior surface of the pons and when it follows caries of the petrous apex, the meningeal signs of cortical bulbar irritation follow symptoms of osseous and dural disease of the middle fossa.

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19 Forks S. B. Gradenigo's Syndrome Arch Otolaryng 7 363 (April) 1928. (Had temporoparietal pain with loss of sensation in the face and external rectus paralysis two years after the ear had ceased discharging and the drum healed.)

# Data on Anatomy of the Sixth Nerve as Presented by Dissections on Nine Cadavers (Seven Fresh and Two Dry)

Dural Portion	First Cadaver	Second Cadaver	Third Cadaver	Fourth Cadaver	Fifth Cadaver	Sixth Cadaver	Seventh Cadaver	Dry Cadavers 00 and 0
Is it adherent to petrous bone?	Dura is part of and continuous to petrous bone, can only be separated by tearing		Left nerve yes by fibrous tissue part of the petrous bone forms the sheath of the nerve	Petrous bone forms a sheath to the nerve on three sides	No	Nerve makes rather a sharp bend over the bone and while it can be separated from the bone there are many adhesions going to the bone	Yes, right trigeminal ganglion slightly adherent to the bone	No but any inflammation of the petrous bone of the apex of the petrous tip would raise the sixth nerve against the occipital condyloid ligament
Is it compressed by canal or not?	No	No	Yes	Could not be easily compressed by elevation of the pons	No	No	Right One branch is in small canal and cannot move freely Left Not so much	Canal so completely surrounds the nerve that it has to be elevated to be seen
Is nerve held to floor?	No	No	Yes	Yes	Left Yes Right No	While it can be separated from the bone there are many adhesions from the nerve going to the bone as it ascends over the tip it is these fibers from the ligament that hold the nerve down	Right Internal branch attached to dura Left Also attached but looser	
Can the nerve be elevated?	Yes	Yes	No	With difficulty, elevation gives the impression that it might easily be compressed against the sharp upper lip of the canal		Moves freely in canal	Right Outer branch moves freely in canal	In Dorello's canal
Does it travel in dural folds?	Yes	Yes	Yes	It is covered by the pia-matroid on the anterior surface of the pons and as it leaves the pons it carries a reflection of pia-matroid			Right Internal branch, cannot move freely in canal but the two branches continue separate into the cavernous sinuses	
Is it on petrous occipital articulation?	Directly at suture		Right nerve is well external to the articulation the bone is on the outer surface for a long distance there being a distinct groove running upward forward and inward	Yes	Yes	Nerve is in the ligament coming from the articulation not in the bone at all it is the fibers from this that hold the nerve down articulation of petrous from occipital easily separated	Left Internal to articulation	00 Right suture widely open but closed line of articulation dim 0 Inside suture uniting petrous pyramid to the occipital
Is the nerve between petrous bone?		Yes	Yes	Yes entire length 3 mm to where it turns forward	Yes		Right Inner branch is on the bone outer branch on ligamentous fibers below the articulation of occipital and petrous Left Outer branch is on the bone at articulation	Rises in canal 0.5 cm passing under the stylo petrous ligament below the posterior condyloid process at the posterior border

Connection of bone cells with those of middle ear	Area is behind eardrum, communicates with middle ear via ossicles. It is continuous with the middle ear via the ossicles. It is continuous with the middle ear via the ossicles.	Large cells in the tip which runs in canal region. Cells extend down canal. Cells are continuous with the middle ear via the ossicles.	Large pneumatic cell directly under the nerve communicates outward to the semicircular canal by a small opening, of the canal at the basal cisterna.	On right side, the petrous part of the temporal bone is very long. The internal branch of the fifth nerve is very long. The internal branch of the fifth nerve is very long. The internal branch of the fifth nerve is very long.	Left: Cell behind petrous tip in Lasserian ganglion communicates by cellular tissue which ends at superior semicircular canal. They are continued forward in front of carotid canal. Cells under middle ear do not reach the region of the middle ear. Right: Bone under sixth cellular does not reach the semicircular canal.	1 cm below inner border of foramen for exit of fifth nerve
Relation of Petrous Cells to Fifth Nerve	Has communication with the carotid canal through cells and is continuous to the posterior and lateral arm of the opposite sphenoid. The tip extends downward under the Lasserian ganglion. Inflammation of bone cells of tip would probably irritate the fifth nerve.	The whole region is so cellular that inflammation of the bone cells of the tip would probably cause irritation of the fifth nerve.				
Distance below inner Margin of Fifth Nerve						



*Data on Anatomy of the Sixth Nerve as Presented by Dissections on Nine Cadavers (Seven Fresh and Two Dry)—Continued*

Bony Portion	First Cadaver	Second Cadaver	Third Cadaver	Fourth Cadaver	Fifth Cadaver	Sixth Cadaver	Seventh Cadaver	Dry Cadavers 00 and 0
Internal to the articulation of the occipital?						Passes to outer part of canal under bony part of petrous		00 Line of articulation hardly visible 0 Internal to suture uniting the petrous pyramid to the occipital
In Passage from Posterior into Middle Fossa								
On which bone does it pass forward?	At the petro-occipital suture	At the crest where it passes from the posterior to the anterior surface on fibrous tissue which unites the petrous pyramid with the sphenoid 12 cm lateral to the ascending wall of the posterior clinoid process			Petio-occipital	Passes to outer part of canal under bony part of petrous only half of nerve being under ligament at all	Left Crosses occipital Right Inner branch is on occipital and petrous outer branch ligamentous fibers	Inside the petrous
Does nerve pass under thin of petrous or not?	Yes	Yes		Yes same condition on the left side where passing is still more visible				
Does nerve turn at right angle or obtuse angle?	Nerve turns at a right angle under the ligament	Turns to a right angle under Gruber's ligament						Beyond Dorello's canal, goes forward in cavernous sinus below postclinoïd process
Direction of Gruber's ligament	Hardly marked, on removing the outer dural layers the nerve passes under the ligament and turns nearly to a right angle	Hardly marked, on removing the outer dural layers the nerve passes under the ligament and turns nearly to a right angle movable	Nerve runs upward and slightly outward under a well developed petrosphenoid ligament which runs markedly upward as well as forward and intersecting the right canal the canal under the ligament is very smooth	Nerve immediately enters a large cavity, the ligament being 0.5 cm away, canal under ligament in the level of the pyramid 0.5 cm long	Left Side Runs upward and inward, well developed under ligament considerable room Right Side Nerve passes under the ligament, appears to divide into two parts at outer attachment the nerve is attached to the internal branch this becomes a part of dura bone cancellous	Well developed direction in and forward with upward direction of about 15 degrees good-sized cavity below ligament nerve is on the ligament coming from the articulation of the ligament 5 mm long	Left Bends under Gruber's ligament in dura, but neither left nor right makes sharp turn Right Gruber's ligament not seen left 8 mm in length in dura	Ligament well seen runs vertically upward and inward sixth nerve passes to outer border with the bone only covered by the perlosteum
Character of ligament at base of petrous	Cancellous one cell	Cancellous	Spongy bone directly under the right nerve	Fibrous tissue fills the space between the petrous tip and the sphenoid old process at base of petrous			Left Bone under nerve spongy petrous tip very large cancellous but in cancellous at base	

<b>Bulbar Portion</b>	Upward in the direction of the posterior clinoid process	Upward in direction of the posterior clinoid process	Upward and inward, right canal slightly lower than the left, direction of the left inward and slightly upward	Left upward and inward, right directly upward	Foramen 45 degrees opening inward, forward and upward	Left Canal runs upward, Right Inner opening, straight up
<b>Length of nerve in bulbar portion</b>		Directly upward so that it lies on the surface of the pons into a network	From which the bulb to entrance into the dura 2 cm			
<b>Size of nerve</b>	Right side Nerve rather large	Right side Nerve rather large	Right nerve large left larger			Right Double, both branches long and frail, in cavernous sinus one branch three times larger than the other Left Rather frail, about size of right, outer and larger upward and slightly inward
<b>Distance between openings into Dorello's canal left and right</b>		2 cm	2.2 cm	2 cm	2.5 cm left on a higher plane than right	Left 1 mm lower than right, Left to right (internal branch) 1.5 cm, (external) 1.7 cm Gives impression of no canal long diameter almost vertical on left side, opening upward and inward, right side is the same but 3 mm lower, diameter 5 or 10 degrees toward sagittal suture, distance between second and sixth nerve, 1.6 cm
<b>Size of opening into Dorello's canal and direction of nerve</b>	Upward in the bone	Right foramen higher than the left direction upward and inward, left almost inward and smaller than the right	Right upward and inward less than 15 degrees from horizontal	Right opening forms an oval slit directly upward	Oval opening inward forward and upward	Left Upward Right Upward and slightly inward Nerve enters canal a long way down canal goes almost directly upward but axis is vertical
<b>Dorello's Canal Portion</b>						
<b>Length of nerve in Dorello's canal</b>		3 mm in the dura, until it passes free into the cavernous sinus	Dural course, 1 mm	Runs up to 3 mm before reaching ligament	1.5 mm in canal before turn	00 Not plain 0 Long, right 2 mm longer than left rises in canal 0.5 cm
<b>On bone or fascia</b>	On bone	Right nerve is on the bone itself	On bone	Left nerve held down to the bone by fascia and runs over the fascia at the articulation the bone can be separated at the articulation		Left In its dural course it was on the articulation above but as it passed over the edge is on the bone, in its dural course is held down by dural fascia

*Data on Anatomy of the Sixth Nerve as Presented by Dissections on Nine Cadavers (Seven Fresh and Two D1y)—Continued*

[illegible]

Consequently the symptoms of localized bulbar meningitis of otitic origin can be summarized as (1) a period with signs of dural irritation of the middle fossa of which facial pain, especially pain behind the eye, is the most significant (possibly associated with abductor paralysis), followed by (2) symptoms of arachnoid inflammation of the posterior fossa near the median line. Localizing middle and posterior fossa symptoms are thus (3) in combination one with the other, (4) semi-coma from which the patient can easily be aroused (5) supine position, on back, with eyes closed, (6) intermittent recurrence of vertical nystagmus. All these are signs of posterior fossa involvement, but without severe headache, great restlessness and opisthotonos of cortical meningitis, although accompanied by high fever and rapid pulse.

(7) Repeated trials of visual fields may reveal great bilateral variations and the sudden appearance of a bitemporal hemianopsia somewhat resembling pituitary tumor pressure.

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# THE NATURE OF EWING'S TUMOR \*

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## INTRODUCTION

From among the reports of cases of malignant tumors of the bone in the Surgical Pathological Laboratory of the Johns Hopkins Hospital representing in all a total of more than 400 cases, a series of 60 cases which were grouped under the name of periosteal round cell sarcoma or Ewing's endothelial myeloma were selected for the present analysis

The result of this analysis has brought forth many interesting and novel features in the natural history and clinical course of this tumor,<sup>1</sup> Under the direction of Dr Bloodgood the cases were first studied microscopically and later correlated with clinical data, the prognosis and ultimate result being made available in fifty-two of these cases by clinical follow-ups

Ewing's sarcoma is essentially a disease of early life, the majority of the tumors occurring during the first two decades (95 per cent) The age incidence ranges between 4½ and 44 years The males affected predominate over the females in an approximate ratio of 2 1, and only one negro was affected in the series

The bones most frequently involved were those of the long pipe bone class, although the ilium, scapula, clavicle, skull and bones of the feet were affected in a few instances In no case was the primary location of the tumor on other than the shaft side of the bone An almost equal number of cases were found divided between the right and the left sides of the body Those bones most readily subjected to trauma were found to be the most frequently affected, that is, the femur, tibia, humerus, fibula and pelvis, the tibia leading the list with involvement in fifteen cases

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1 Copeland M M and Geschickter C F Ewing's Sarcoma Arch Surg  
20 246 (Feb) 1930

## SYMPTOMS

Trauma was recorded in twenty-two cases and in every instance was definitely related to the subsequent onset of clinical symptoms. The average latent period noted between the time of trauma and the clinical onset of symptoms was approximately five and one-half months.

Pain was an outstanding symptom in fifty cases (83 per cent) and was noted as the first symptom in twenty-one cases (35 per cent). It usually began spontaneously, though in some cases it followed trauma and tenderness by a more or less short period, often appearing simultaneously with tumor formation. Most frequently the pain was first intermittent, lasting from a few hours to several days, subsiding at intervals but recurring each time in a more severe form. The intervals between the attacks appeared to become shorter in duration, until a constancy of pain was noted by the patient. Nocturnal pain was found to be the most severe in many cases.

In fifty-six cases (90 per cent) a mass could be palpated, and in 19 per cent of the cases it was complained of by the patient as the initial symptom. The average duration of tumor formation, as noted by the patient before coming under observation, was thirteen and one-half months. The tumor masses varied from small localized swellings to large fusiform masses, extending along almost the entire length of the affected bone. Peripheral disturbances about the tumor were manifest in the form of vasomotor changes, often giving the skin a somewhat more red or bluish tint than that of the surrounding cutaneous areas. The soft parts, though usually freely movable were often edematous. In many instances recorded, local elevation of temperature was found over the tumor mass. On palpation the tumors usually presented a hard indurated swelling, apparently continuous with the sheath of the bone. Fluctuation of the tumor was not noted, though there were varying degrees of resilience, all the growths being less hard than bone.

In some of the tumors there was a tendency to decrease spontaneously in size, with sudden cessation of pain. The variability in the size of the tumor is to be associated with hemorrhage and its absorption.

Pathologic fracture was of relatively rare occurrence, being noted in only three cases (5 per cent) in the series. Two fractures were in the upper shaft of the femur and one in the lower shaft.

As was pointed out in a previous communication, among the malignant tumors of the bone, the greater number of pathologic fractures (62 per cent) are found in association with multiple myeloma, while other types similarly affected by fracture are, in the order of their frequency: bone cysts, 45 per cent, giant cell tumor, 14 per cent, and

osteogenic sarcoma of the bone, 8 per cent <sup>2</sup> Thus, among the types of tumor of the bone complicated by pathologic fracture Ewing's sarcoma presents the minimum number of cases

The constitutional reaction of the body to tumor invasion reveals a variable response in different patients

The range of temperature elevation is between 99 and 104 F, the average being 100 These elevations in temperature were commonly observed late in the disease after metastases had occurred, but fever was also noted early in the clinical course in 30 per cent of the cases A slight albuminuria together with a few white and red blood cells in the urine was often associated with the fever Though Bence-Jones bodies were not sought as a routine procedure in this series of cases, these bodies were not found in a single instance when the test was carried out <sup>3</sup>

In thirty-one cases in which complete blood counts were made, the blood picture ranged from that of the normal type to that of a secondary anemia and from a relative leukopenia to a considerable leukocytosis The white blood count and its differential count presented no unusual peculiarities Twenty cases showed more than 10,000 leukocytes and three had a count of 20,000, the average in these cases being 15,200 white blood cells, this is often a source of confusion leading to the diagnosis of osteomyelitis The differential count, except for an occasional eosinophilia ranging from 4 to 20 per cent, was within normal limits

The patients showed great variability in nutrition In some cases a noticeable loss of weight was observed early in the course of the disease over a relatively short period, while in other cases there was little or no evidence of undernutrition until near the termination of life The terminal phases of the disease revealed a progressive emaciation in most of the patients observed

Internal metastases usually present themselves clinically late in the disease

As seen by the x-ray, Ewing's sarcoma is most often diffuse and is situated near the midshaft of a long bone The earlier lesion presents the more difficult diagnosis, and in this disease the difficulty is enhanced by the variability in the appearance of the bones affected and infiltrated by the tumor The neoplasm expands the shaft of long bones by a diffuse infiltration of the region which results in widening and increased density of the cortex and a mottling of the marrow cavity, due to areas of increased density Both new bone formation and bone destruction are secondary to infiltration of bone by the tumor

<sup>2</sup> Geschickter C F and Copeland M M Multiple Myeloma Arch Surg 16 807 (April) 1928

<sup>3</sup> Rogers and Guthrie Am J M Sc 144 803 1912



(fig 1) In the early case, bone formation predominates, giving rise eventually to either parallel or radiating spicules of new reactive bone. In the later stages of the disease bone destruction, both medullary and cortical, characterizes the x-ray picture.

The roentgen studies presented here do not support the view that Ewing's tumor is a lesion that is primarily destructive of bone,<sup>4</sup> in six of seven early cases the first evidence of tumor infiltration was an

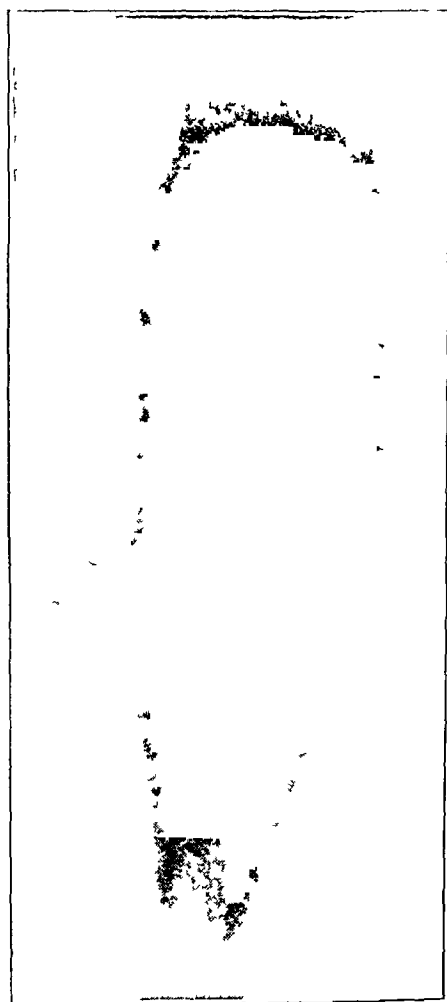


Fig 1—A roentgenogram showing bone formation and bone destruction. The periosteal reaction with parallel layers of reactive bone, characteristic of early Ewing's sarcoma, should be noted.

increased density of the bone. The typical contour of the involved area in the bone is also against the current conception of the medullary origin of this neoplasm. On a physical basis, one would expect medullary tumors to show an approximate spherical shape in the roentgeno-

<sup>4</sup> Ewing, J. Neoplastic Diseases, ed 3, Philadelphia, W. B. Saunders Company, 1928.

gram, because their expansion is unhindered in three and usually in four directions. In contrast to this, the area infiltrated by Ewing's tumor is generally elliptic, with its long axis parallel to the shaft of the bone, indicating that the growth is resisted in the two opposite directions.

#### PATHOLOGIC CHANGES

An analysis of the gross pathologic changes aids materially in the interpretation of the roentgen observations. The tumor is usually



Fig. 2—A gross specimen in longitudinal section showing the primary involvement of the shaft with secondary invasion of the epiphysis. It should be observed that the bulk of the tumor is beneath the periosteum and outside the cortical region.

located on the metaphyseal side of the bone, the epiphysis being secondarily involved in only three instances. Regardless of the site of origin of the tumor, all the gross specimens with one exception showed the bulk of the tumor lying subperiosteally (fig. 2). The medullary cavity in some instances contained a small portion of the tumor, but usually this region was constricted or totally occluded by new reactive bone (fig. 3). The widened cortex as pictured in the roentgenograms

is shown in the gross specimens to be made up of subperiosteal and endosteal new bone formation, which encroaches on the medullary space and frequently seals it off from tumor invasion. The tumor appears to infiltrate rather than to destroy bone in its early stages, and the bone thus infiltrated reacts vigorously with new bone formation, but this bone may subsequently undergo destruction when surrounded and infiltrated by tumor, apparently because of the interruption of the blood



Fig 3—A gross specimen in longitudinal section showing endosteal reaction, which is sealing off the medullary cavity by reactive bone in an attempt to overcome tumor invasion

supply where the tumor has invaded and blocked both the Volkmann's and the haversian canals (fig 4)

When the involvement of the bone by the tumor is diffuse, the subperiosteal reaction of new bone formation is both parallel and at right angles to the cortex. The origin of this bone is explained by the

mode of advance of the tumor through the haversian system and Volkmann's canals. The parallel deposits of new bone appear to be the result of bone proliferation from the subperiosteum and peripheral layers of the cortex, when the periosteum has suffered minute separation from the cortex, giving an onion peel-like formation characteristic of the early roentgenographic appearance (fig 1). With increased separation of the periosteum, spicules of new bone arising either from the cortical region or from beneath the periosteum are laid down at



Fig 4—A gross specimen taken late in the disease, showing the ultimate destruction of the cortical bone, apparently due to interruption of the blood supply where the tumor has invaded and blocked both Volkmann's and the haversian canals.

right angles to the shaft rather than parallel (fig 5). We<sup>5</sup> agree with Ribbert that this fact is due to the vessels perforating Volkmann's canals, which determine the direction of the new growth of bone when

<sup>5</sup> Buerger L. Further Studies of Sarcoma of Bone, *Am J M Sc* **140** 355 1910

they are pulled outward in maintaining their continuity with the periosteum, after it has been elevated. This determination of bone pattern by vessel units is typical of the embryo and is not lost in the adult. The soft part tumor is usually encapsulated by a thin layer of fibrous tissue, which at the margin of the growth is seen to be continuous with the periosteum. The tumor tissue itself is a firm but granular, grayish-white substance divided into characteristic lobules by

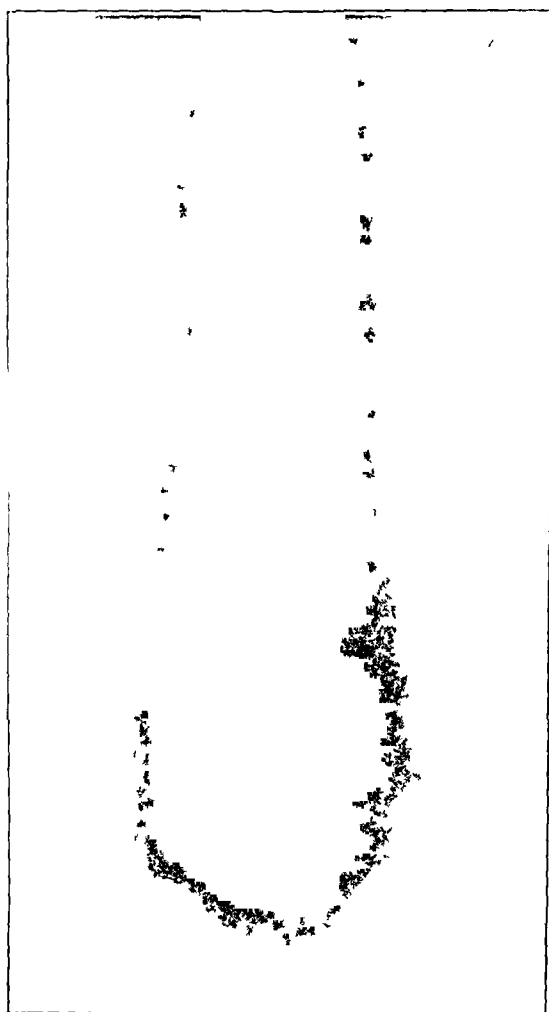


Fig 5—Roentgenogram of Ewing's sarcoma showing osteophytes at right angles to the cortex, together with a thickening of the cortical bone. It should be noted that this reaction is diaphyseal in location.

a number of connective tissue strands, extending from the outer capsule to the region of cortical bone. Occasionally, cysts are noted in the tumor substance.

The microscopic pathology is one of the most uniform characteristics of the disease, revealing a more or less constant cellular morphology. The type of cell in compact areas is small and polyhedral, with a

round or oval nucleus (fig 6) The cytoplasm is quite scanty and practically stainless The nucleus is deeply stained, showing a definite limiting membrane with a sparse number of chromatin granules scattered through the nucleus without definite arrangement Nucleoli are rarely seen, but mitotic figures are frequently noted Little pleomorphism is observed, and multinucleated cells of tumor origin have not been noted this being an important matter in the microscopic diagnosis

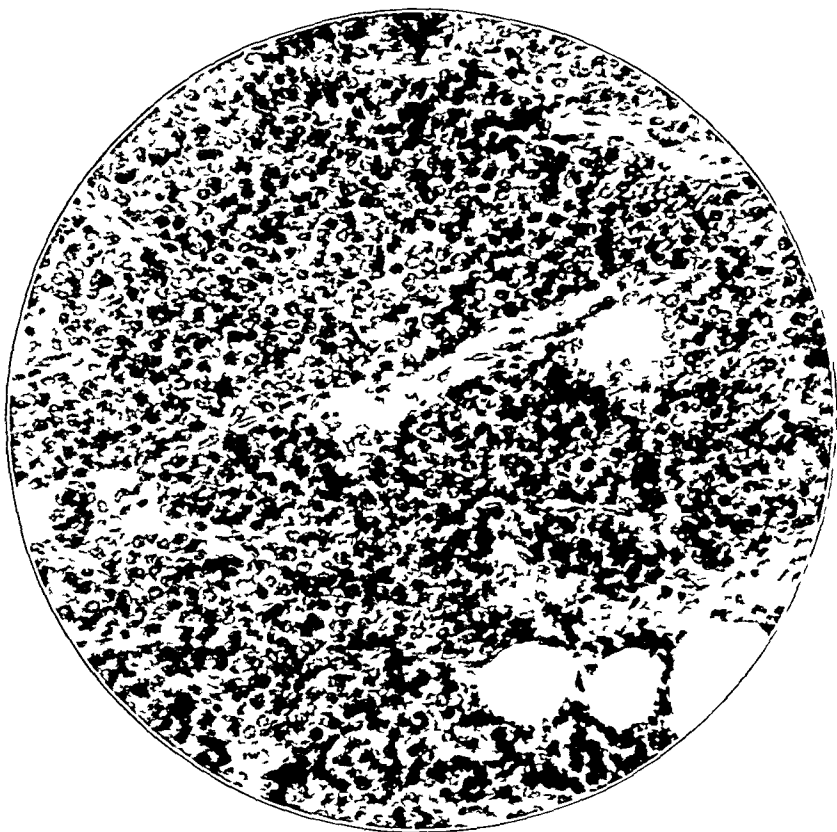


Fig 6—Photomicrograph showing the uniformity in the size of the cells and the indistinct cytoplasm with round and oval nuclei

There appears to be no intercellular stroma in the tumor (fig 7), but fibrous trabeculation divides the neoplasm into lobules, where it is found subperiosteally These septums often give the tumor an alveolar arrangement

Vascularity is variable in these tumors and may be pronounced In some sections taken through areas of bone haversian canals occupied by blood vessels were infiltrated by the tumor the tumor cells sometimes lying within and sometimes without the vessel walls (fig 8)

Phenomena of this character have been cited by some authors as evidence of the seat of origin of the tumor, but we are inclined to the belief that in most of these instances tumor cells are following the path of least resistance in their invasion of bone, traversing the haversian systems

Areas of fibro-ostosis<sup>6</sup> (osteitis fibrosa), either subperiosteal or endosteal in origin, are seen where the tumor is invading bone, and constitute a healing reaction (fig 9)

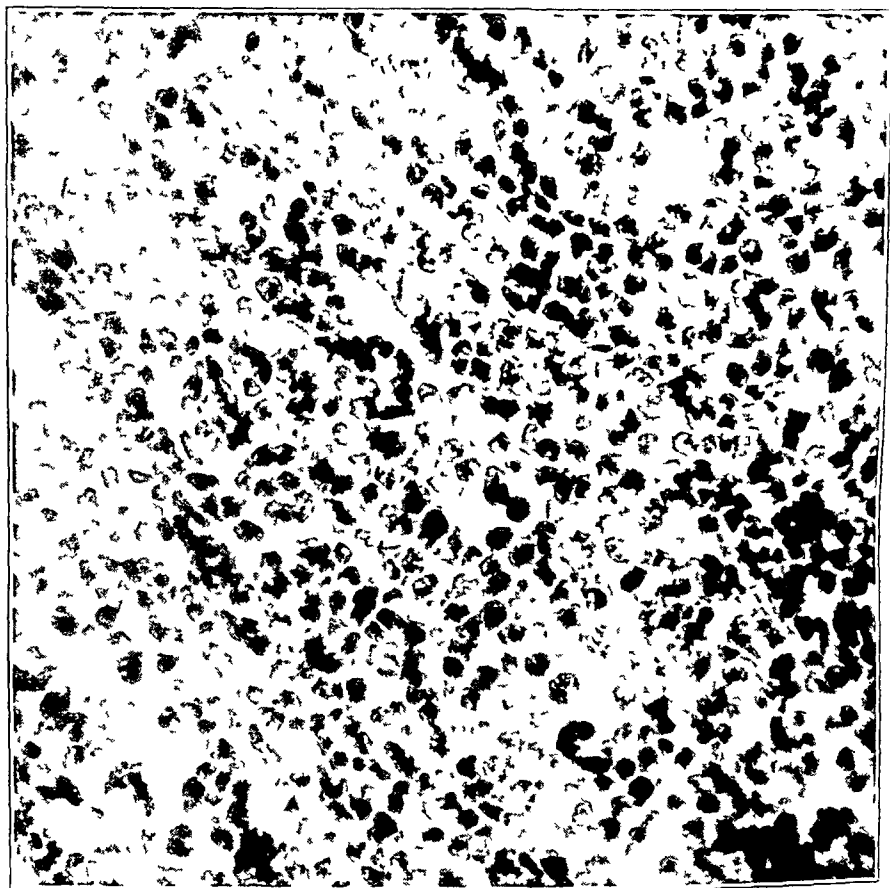


Fig 7—Photomicrograph of Ewing's sarcoma. Observe the lack of intercellular stroma

Necrotic areas of tumor are often noted surrounding islands of tumor cells through the center of which a blood vessel passes, the blood supply apparently being inadequate for more than the tumor cells immediately surrounding the vessel. The periphery of these tumors is frequently infiltrated by cells of the polymorphonuclear or monocytic types. This round cell infiltration is most common in the tumors of

<sup>6</sup> Geschickter, C. F., and Copeland, M. M. Osteitis Fibrosa and Giant Cell Tumor. *Arch Surg* 19: 169 (Aug) 1929

longer duration or in those which have previously been explored and not infrequently leads to an erroneous diagnosis of osteomyelitis at biopsy. Plasma-like cell infiltration was noted in a few cases and this possibly may have no special relation to the tumor, as sections of normal bone sometimes show such cells. On the basis of finding these cells, certain authors have suggested a relation between this tumor and multiple myeloma.



Fig 8—Photomicrograph showing a portion of the cortex of a bone. The haversian canals have been widened by the infiltration of tumor which has pervaded the bone by means of the perivascular lymphatics within the haversian canals.

Dissemination and metastases have occurred in every case of the series which so far has terminated fatally. The extent of metastases

7 Ewing (footnote 4) Kolodny A Bone Sarcoma Surg Gynec Obst  
44 126 1927



has been most difficult to localize because of the insufficient data included in many of the case reports, while necropsy has been performed relatively rarely in the series. Only those fatal cases in which there has been definite proof of metastases have been reported in this discussion although every patient is said to have died of tumor. The most frequent sites of metastases are the lungs, the lymph glands and the skull.<sup>3</sup> The most unique feature in the dissemination of Ewing's tumor

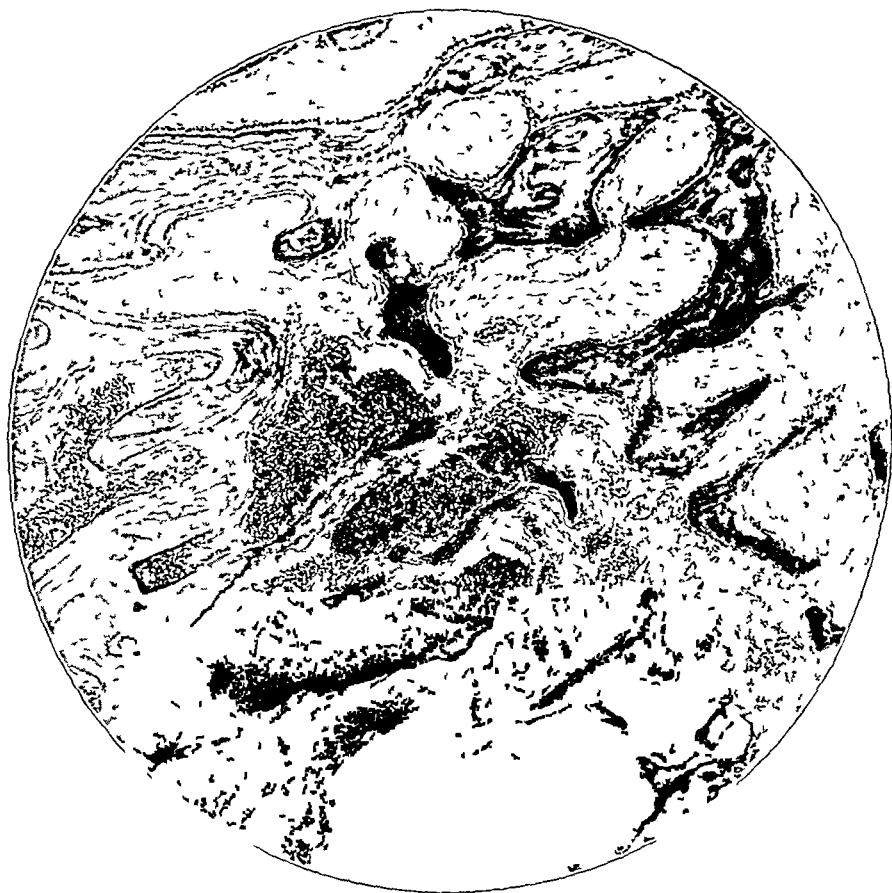


Fig 9—Photomicrograph showing osteitis fibrosa surrounding the area of tumor invasion. Observe the osteoid spicules surrounded by osteoblasts and fibrous tissue. See figure 1.

is the predilection of the secondary growths for other bones. Though some observers view this dissemination to other bones as a proof of the fact that the tumor is primarily a multiple disease of the skeleton, in our series it was nearly always possible to obtain a definite latent period of from two and a half months to a year between the appearance of the tumor in the single initial bone and the secondary involvement of other bones.

The bones most frequently involved by metastases are the skull spine, scapula and clavicle although dissemination may occur in the long pipe bones

Though the involvement of the single bone early in the disease with later dissemination of the neoplasm to other bones constitutes a unique and important feature of the disease, it is unusual for the patient to present himself for examination with more than one bone involved, and a single focus usually predominates in size as well as in the duration of its growth

In reviewing the many diagnoses first made and later revised in cases of Ewing's tumor, it is interesting to note that inflammatory diseases of the bone predominate. A primary diagnosis of pyogenic periostitis or osteomyelitis was made in ten cases, tuberculous disease of the bone in nine cases, syphilitic periostitis or osteomyelitis in six cases and typhoid osteomyelitis in one case, thus showing the frequency with which Ewing's tumor is confused with chronic inflammation of the bone. Clinically, multiple myeloma was noted as a source of confusion in two cases, and literature on Ewing's sarcoma involves osteogenic sarcoma and metastatic carcinoma as sources of confusion. Since space here does not permit going into a differential diagnosis of Ewing's sarcoma suffice it to say that biopsy is most often resorted to in making the diagnosis (fig 10)

At the present time we have complete follow-up reports in fifty-two cases of Ewing's sarcoma. Forty-three of the patients are dead and eight (13 per cent) are living and apparently well, with an average duration of life of seven years and eight months following the initial symptoms

#### TREATMENT

We have divided the methods of treatment into three main groups for analysis. (1) amputation or resection with irradiation, (2) amputation or resection without irradiation, and (3) irradiation alone or with exploratory operation

In group 1 are thirteen patients in whom the postoperative duration of life averaged 29.2 months, three (22 per cent) of this group are well, with an average duration of life extending over a period of five years and seven months

In group 2 are twenty-four patients with an average duration of life extending over a period of twenty months, four (16.5 per cent) of this group are well, the average duration of life extending over a period of six years

In group 3 are eight patients with an average duration of life of twenty-seven months. One patient of this group is living after fifty-three months curettage having been performed prior to irradiation

Coley's toxins apparently have had no effect on the duration of life, whether the toxins were given alone or were combined with other forms of treatment

The weight of evidence at this time seems to indicate that the patient should receive the benefit of both radical operation and roentgen treatments when the tumor is observed in the usual location prior to the formation of metastases<sup>8</sup> Exploration does not necessarily affect

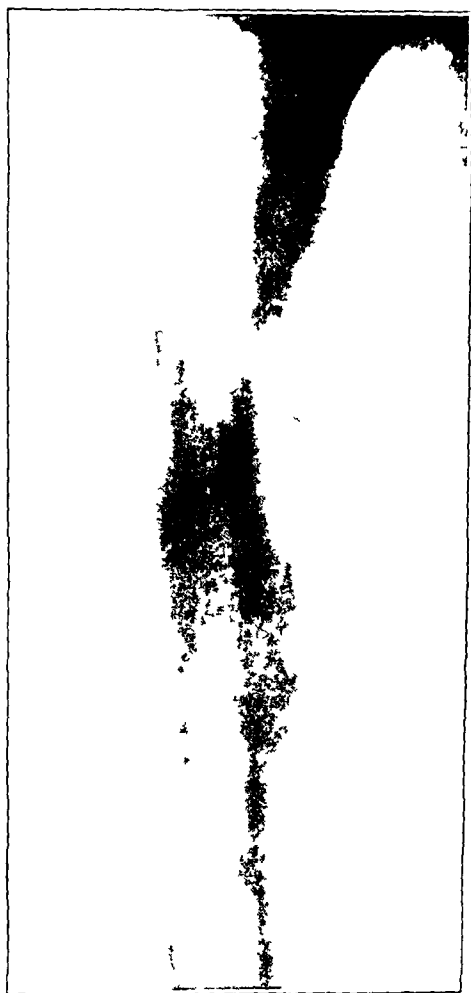


Fig 10—A roentgenogram of Ewing's sarcoma in the femur which is not unlike early inflammatory disease of the bone

the prognosis of the disease when radical operation or roentgen treatment follows this procedure In two patients living after five years, exploration was done before the operation of choice was resorted to In six cases in which exploratory operation without further treatment

<sup>8</sup> Bloodgood J C Bone Sarcoma Periosteal and Diffuse Type and their Diagnosis from Benign Lesions, J Bone & Joint Surg 8 727, 1926

was performed, death occurred in from one to twenty-two months. One patient who received Coley's toxins alone died fourteen months after the therapeutic procedure was begun.

#### COMMENT

When the facts brought out by the analysis of this series of cases are listed, they point to the conclusion that the tumor is a malignant sarcoma of the bone. In favor of this is the age incidence of the tumor, its location in bone, the cellular nature of the pathologic changes, the metastases and the high percentage of fatality. Against the opinion that this lesion is a metastatic tumor arising primarily outside of bone is the failure to demonstrate such a primary focus in any of the cases studied, the cellular morphology of this tumor does not resemble that of carcinoma, nor does the age of the patient suggest such a disease. The cures effected by amputation or the resection of a single bone are also against this assumption.

The summary of our investigations is also against the belief that the tumor is possibly a myeloma originating in the marrow cavity. In the first place, the elliptic area of involvement of the shaft with the bulk of tumor lying subperiosteally does not resemble the usual central and spherical contour of medullary tumors. Multiple myeloma, metastatic carcinoma and chloroma with leukemia all show a central location with a more or less spherical growth widening the medullary cavity. These tumors occupying the marrow cavity show early bone destruction and in the majority of them Bence-Jones bodies have been demonstrated during the course of the disease. Ewing's tumor, in contrast to these neoplasms, most frequently shows a narrowing or occlusion of the medullary cavity with both endosteal and subperiosteal new bone formation early in the disease, which would seem to indicate that the tumor has not a primary medullary origin. The absence of marked changes in the blood picture and Bence-Jones bodies in the urine is also against this assumption. Examination of gross specimens and microscopic sections cut transversely through the bone usually shows only a small portion of the tumor tissue in the marrow cavity, the rapid extension of the tumor in a plane parallel to the axis of the shaft indicates that the neoplasm is not able to expand freely in a central or peripheral direction, thus pointing to the fact that the growth is either intracortical or subperiosteal in origin.

The majority of the observations could be explained by either an intracortical or a subperiosteal origin of the tumor. If the neoplasm were primary in the haversian systems, this would explain the rapid infiltration of the tumor producing early endosteal and subperiosteal reactions of new bone. It would explain also the distribution of the tumor under the periosteum and into the medullary cavity in the later

stages, and account for the widening of the haversian canals and the splitting of the layers of the cortical bone so frequently observed under the microscope. However, conclusive microscopic proof for the origin of Ewing's tumor in the haversian canals is lacking. While all specimens usually show the tumor pervading these structures we have been unable to tell whether the tumor arises here or secondarily infiltrates into these channels. The assumption that Ewing's tumor arises in the subperiosteal location may be maintained with probably equal validity from the facts observed. The active subperiosteal layer which ceases at the epiphysis and atrophies in adulthood would account for the primary involvement of the shaft only, in the bones of youthful patients. This locality would account also for the fact that the bulk of the tumor is to be found under the periosteum, for the tendency of the haversian system to be infiltrated and for the reactive new bone formation of both endosteal and subperiosteal origin. It would explain also the tendency of the tumor to extend up and down the shaft rather than to form a spherical growth. It would also fit in with the absence of Bence-Jones bodies in the urine and the lack of marked changes in the blood picture.

On the basis of the observations that have just been pointed out, it is clear that whether the tumor is primarily intracortical or subperiosteal, it is evidently not medullary or primarily osteolytic, as is currently believed. The rarity of pathologic fracture, the localities affected and the results of roentgen and gross examinations are all against this assumption, and bone destruction is always a late manifestation of the disease.

Perivascular lymphatics in bone have been suggested by some as a possible source of origin for the tumor. This is not altogether unfeasible and would give this tumor an intracortical origin.<sup>9</sup> Although tumor cells are frequently observed about the vessels in the haversian canals, sections of normal bone do not show cells of the Ewing type from which the neoplasm might arise. While we have observed proliferation of cellular elements about these lymphatics of bone beneath such conditions as bursitis, the cells are of a different type and the endothelium of the lymphatics does not appear to us to resemble Ewing's cell. We have reviewed the endotheliomas of the soft parts along with all the sarcomas of the soft parts in the surgical pathologic laboratory and do not find a tumor duplicating Ewing's sarcoma in morphology.

The facts at our disposal at the present time do not enable us to point out either the site of origin or the histogenesis of this tumor, and while we believe that the primary focus is specific for bone and is probably intracortical or subperiosteal we prefer to leave the matter sub judice.

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<sup>9</sup> Ewing, J. Endothelial Myeloma of Bone, *Proc. New York Path. Soc.* 24: 93, 1924.

# ISCHIORECTAL PROSTATECTOMY \*

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Any operative procedure having as its fundamental precept the removal of a pathologic structure with due regard to its physiology and to the preservation of the related anatomy should find itself within the capabilities of every well trained surgeon.

The division of opinion of surgeons throughout the world as to the choice of method in prostatectomy indicates that except to a brilliant few neither the suprapubic nor the perineal method with its various modifications fulfils all requirements. The choice of one method rather than the other because of greater familiarity with the procedure and the constant attempts to vary and improve the technic are proof of a somewhat general dissatisfaction.

It was this dissatisfaction which led Voelcker after many years experience with both the suprapubic and the perineal methods and their various modifications, to present before the Berlin Surgical Congress in 1919, the technic of his ischiorectal prostatectomy with a report of fifty-six cases in which this operation was performed.<sup>1</sup>

He felt that the difficulties in hemostasis and in the after-care of the wound in the suprapubic operation and the technical difficulty of gaining adequate exposure by the perineal method were definite faults of these operations.

At that time, he made the following apt comparison:

Compare for example the marked variance of our surgical principles in performing cholecystectomy and prostatectomy. When we remove a gallbladder filled with stones we do not simply loosen it from its bed by blunt dissection and then tear it in two at its neck. Rather do we carefully make our peritoneal incision, and gently free the bladder, taking the utmost care not to injure the liver and the adjoining structures. We then ligate the deeper vessels, carefully clamp and ligate the cystic duct and cover it again with peritoneum or, when we are uncertain of the desirability of primary closure, a drain is carefully placed in proper position.

In prostatectomy, however, the gland is freed by blunt finger dissection, in part not under the guidance of the eye, and is then torn from its surrounding structures.

\* Submitted for publication, Sept. 6, 1929.

<sup>1</sup> From the Chirurgische Universitätsklinik und Poliklinik, Universität Halle-Wittenberg, Prof. Fritz Voelcker, Director.

<sup>1</sup> Voelcker, Fritz. Die Prostatectomie als gut übersichtliche Operation, *Ztschr. f. urol. Chir.* 4: 253, 1919.

The ischioirectal method has the following distinct advantages

1 The entire operation is done under the guidance of the eye, the anatomic structures being readily recognized and respected

2 Exact hemostasis by means of ligature, suture and packing is possible, the bleeding points being readily seen

3 The bladder neck and the internal sphincter are clearly seen, and so the possibility of leaving small pieces of adenoma behind is unlikely

4 Dependent drainage from the base of the wound is obtained

5 Death from shock has not occurred in 148 cases observed, this hazard being given by most writers as the third most important cause of death

6 Permanent fistula or incontinence has not occurred

The technic of the operation has been simplified in many small details in the last ten years. The procedure as described here seems not to have found its way into the American literature

#### METHOD

*Preparation*—Every effort is made to have the patient in the best possible preoperative condition. Preliminary drainage is made with either the indwelling catheter or the suprapubic fistula, as indicated. Preliminary vasotomy is considered an essential part of the preoperative preparation, and its performance is urged whenever possible before treatment with the indwelling catheter is inaugurated. Postoperative epididymitis is a frequent and most unpleasant complication. Young<sup>2</sup> reported this complication in 20 per cent, Davis<sup>3</sup> in 13 per cent and White<sup>4</sup> in 57 per cent of the prostatectomies performed by them. More than 30 per cent of a former series in this clinic developed epididymitis, but in the present series of 148 cases, all with preliminary vasotomy, this complication did not arise.

*Position of the Patient*—The patient is placed in the prone position with the head and chest about 12 inches lower than the pelvis. A round leather hair pillow is placed across the lower part of the abdomen and strapped to the thighs by means of a pole running through its center, the pressure is so exerted as to force the lower abdominal organs dorsalward. The legs are widely spread about the two uprights of the operating table and the feet encased in specially constructed stirrups (fig. 1).

In my experience, the percentage of postoperative pneumonia is not increased through the use of this position. Patients who are operated on under spinal anesthesia do not complain of discomfort from the position.

*Incision*—A small sponge is sewed over the anus with a purse-string suture. The incision is made over either the right or the left ischioirectal fossa, according to the preference of the operator. Usually the incision is not longer than 10 cm,

2 Young, H. Prostatectomy, Pre-Operative, Operative, and Post-Operative Treatment, Surg. Gynec. Obst. **36** 589, 1923.

3 Davis, Edwin. Perineal Prostatectomy, J. A. M. A. **91** 1618 (Nov. 24) 1928.

4 White, H. P. W. Epididymitis and Supra-Pubic Prostatectomy, Lancet **202** 321 1922.



Fig 1—The position of the patient (This and the accompanying illustrations are taken from the monograph of Fritz Voelcker and H. Boeminghaus, *Anatomie und chirurgische Operationslehre der Prostata* in *Handbuch der Urologie*, Berlin, Julius Springer, 1926, vol 1. This is figure 25 p 232 of the handbuch.)

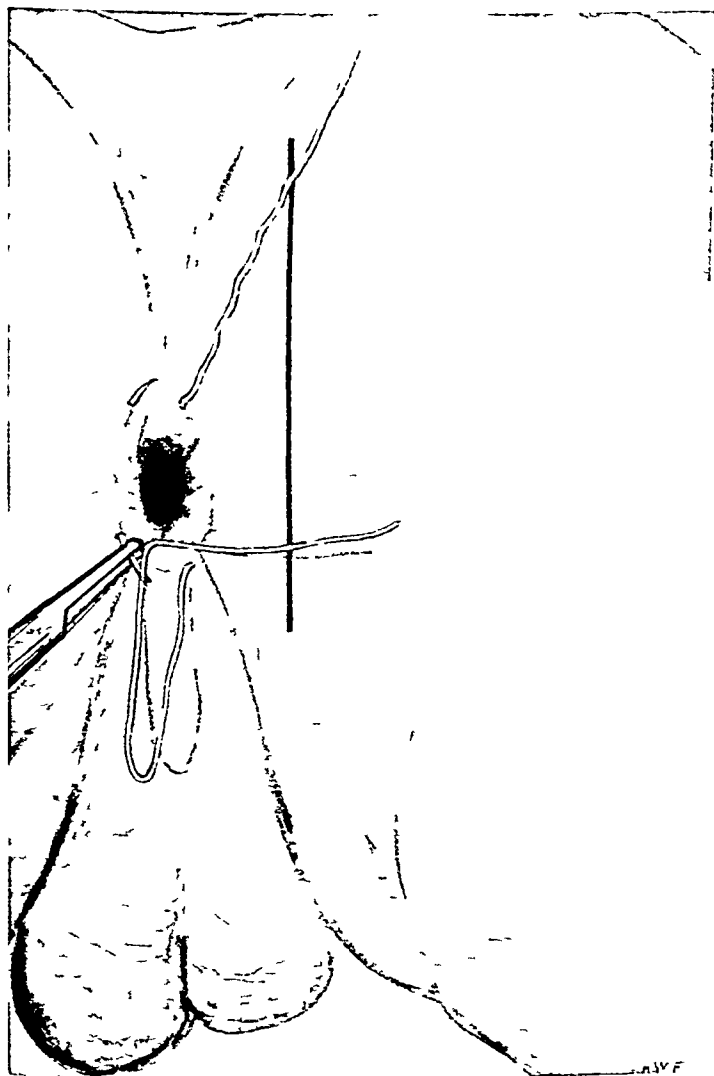


Fig 2—Incision



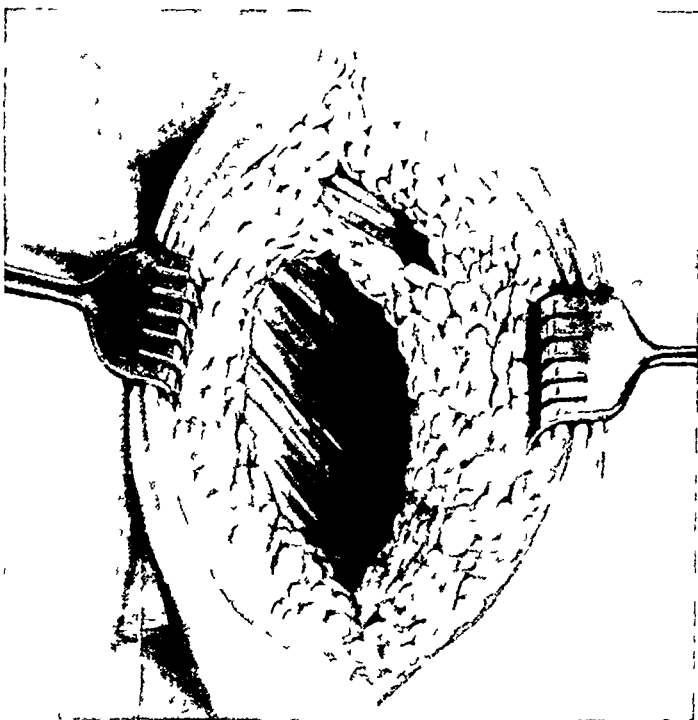


Fig 3—The levator ani is exposed and the direction for its incision is shown. The inferior border of the gluteus maximus is seen in the upper border of the wound (fig 26, p 233)

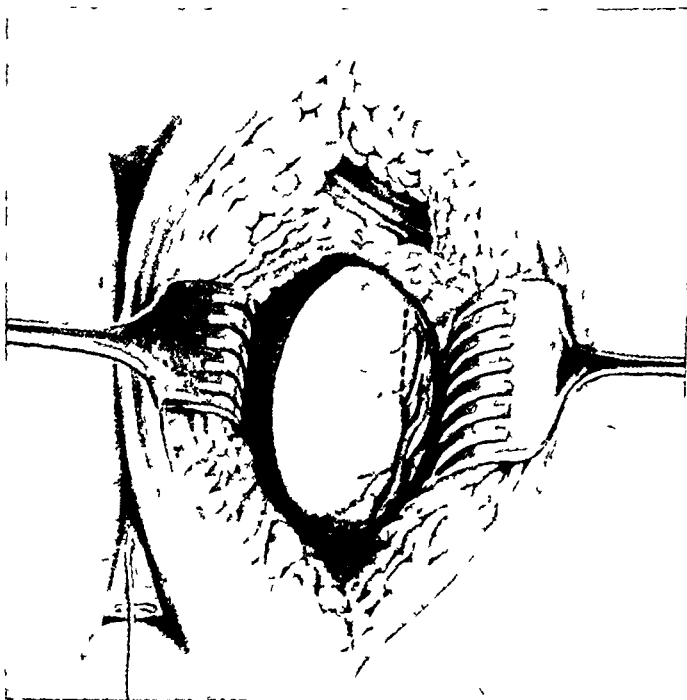


Fig 4—The levator ani is divided and retracted. The membrana pelvis visceralis, the accompanying venous bundle and the line of incision are shown (fig 27, p 233)

starting at the sacrococcygeal articulation 3 or 4 cm. from and parallel to the midline and extending to or a little beyond the anus.

The skin and superficial fascia having been incised the thick gluteal fat pad is divided in the same direction as the skin incision the branches of the inferior hemorrhoidal artery being ligated as they are met. The small motor nerve branches running to the anus may be cut without fear of weakening the sphincter control. At the upper border of the incision appears the gluteus maximus which is left untouched. The fat bolster having been incised the levator ani muscle which lies directly beneath it is also incised parallel with the midline and retracted to either side (fig. 3). Below this muscle is the membrana pelvis visceralis which is readily recognized by its shimmering whitish color.

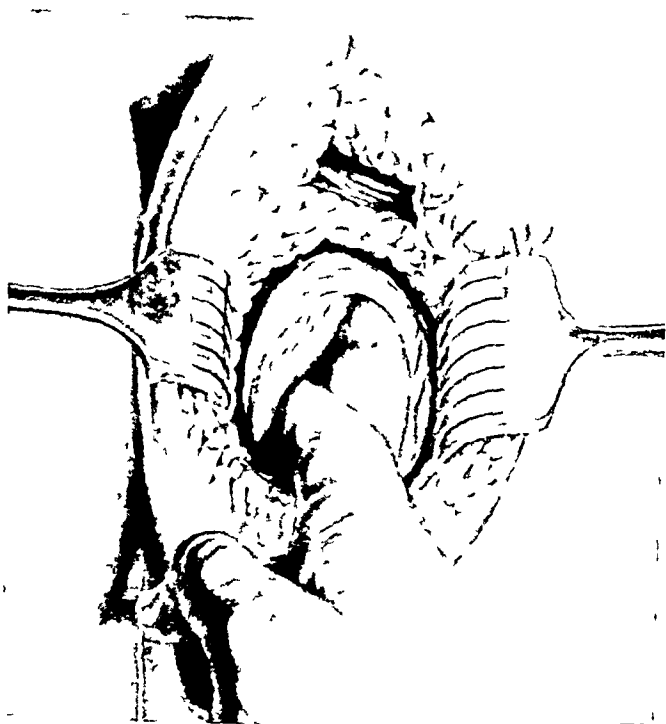


Fig. 5—The membrana pelvis visceralis has been incised and the prostate is being separated from the rectum by blunt finger dissection (fig. 28, p. 234).

The next step may be termed the crucial one of the operation, for the deliverance of the prostate without wounding the rectum depends on the careful separation of the prostate and the rectum. These structures are bound together, from the surgical standpoint, by this rather thick layer of tough connective tissue. Fortunately, at this point there is a constant landmark in the form of a readily recognized group of veins running parallel to the anterior rectal wall. At times they lie some distance laterally and quite deep in the incision, being seen only after the cut half of the levator ani has been adequately retracted.

As these veins indicate the plane of cleavage between the prostate and the anterior rectal wall, the membrana pelvis visceralis is incised, millimeter by millimeter, slightly medial to these veins and deep enough that the incision may be widened by gently tearing this structure with the two index fingers (fig. 4).

The prostate and rectal borders are now definitely felt, and the finger is easily inserted into the plane of cleavage between them. Keeping always along the posterior prostatic surface, the operator can easily separate the anterior rectal wall from the prostate (fig 5). The freed rectum is then retracted with a

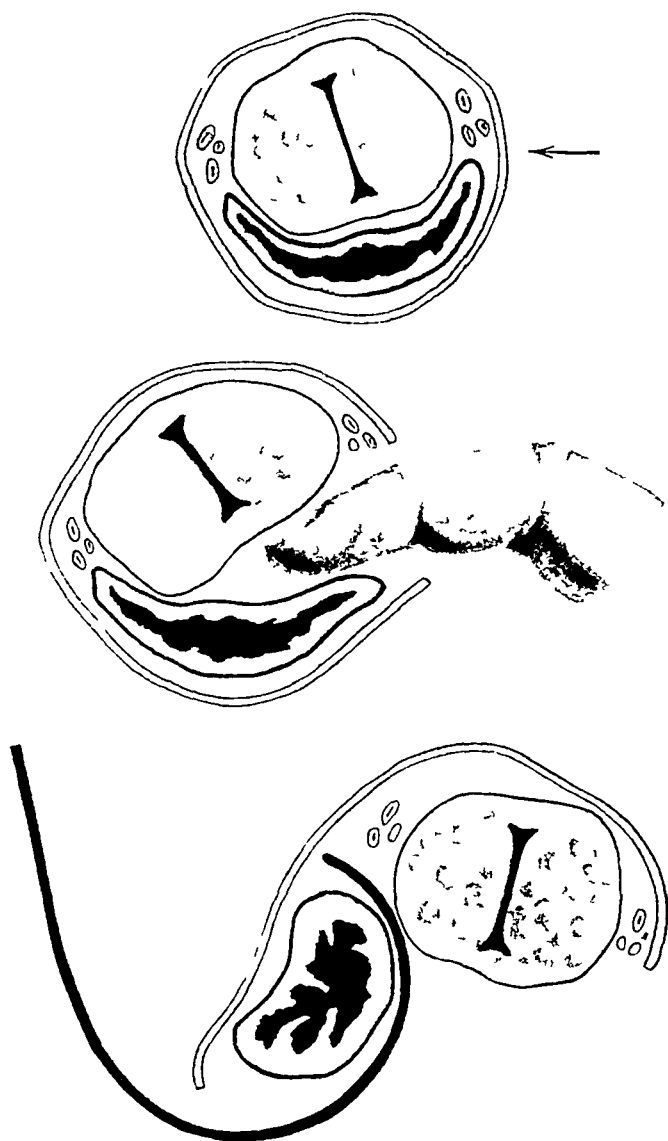


Fig 6—Diagrammatic representation of the relation of the rectum and the prostate during the freeing of the latter (fig 32, p 237)

specially constructed, broad, sharply curved retractor, leaving the prostate in full view (fig 6).

During this part of the operation the operator should remember that the enlarged prostate has cupped itself about the collapsed rectum, distorting it into a definitely crescentic form (fig 7). Those who are unfamiliar with the technic may insert a light into the rectum as an added safeguard.

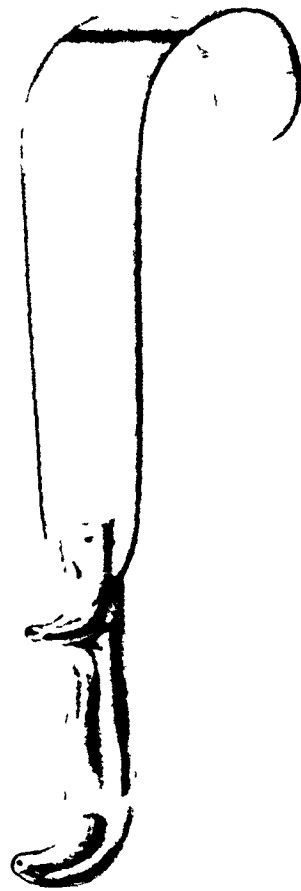


Fig 7—The rectum retractor (after Volckner) (fig. 33 p 237)

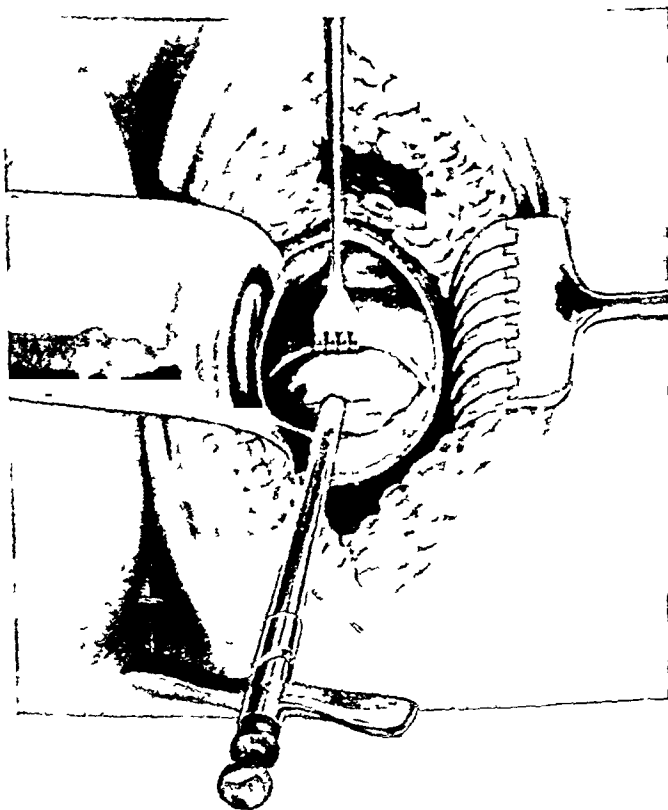


Fig 8—The prostatic sheath and the prostate have been divided horizontally.  
A Young retractor has been inserted through the prostatic incision (fig. 29 p 235)

## REMOVAL OF THE PROSTATE

A horizontal incision is now made through the prostatic sheath and the hypertrophied gland, about 1 cm distal to its center, the incision penetrating into the prostatic urethra (fig 8). The tip of the indwelling catheter is delivered into the wound, a Young retractor is inserted through the urethral opening, its blades are opened, and the gland is pulled gently forward and downward, the operator now recognizing the neck or base of the bladder. The prostatic sheath (the so-called capsule) is then freed with the scissors from the upper half of the divided gland until it may be held aside with a small claw retractor, the gland then being freed further by blunt finger dissection. In the region of the seminal vesicles, however, the dissection should be sharp throughout, since these structures may be readily injured by too brusque blunt dissection.

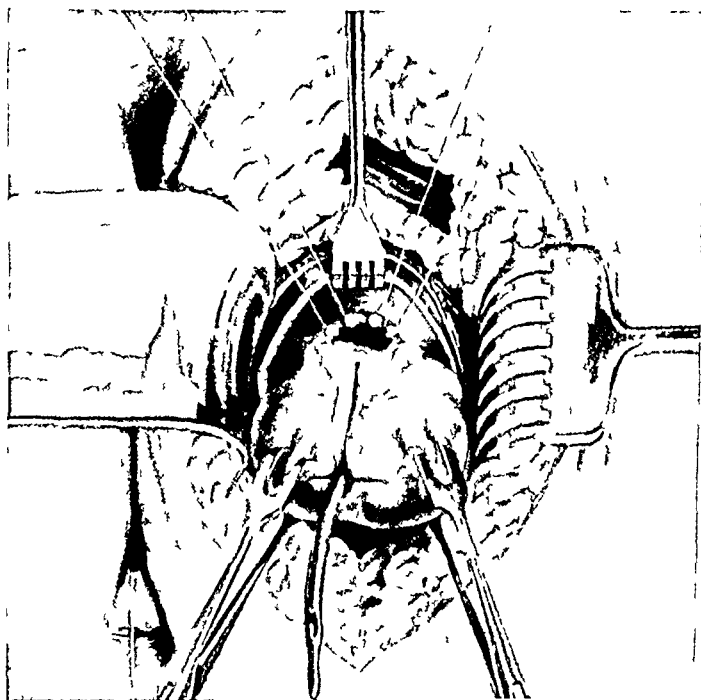


Fig 9—The prostate, having been divided longitudinally, is being cut from the bladder neck, sutures in the latter being tied to prevent bleeding. Grasping forceps have been substituted for the Young retractor. The indwelling catheter has been led out through the original prostatic incision (fig 30, p 236).

The gland is now cut from the bladder neck with the scissors, the surgeon cutting and suturing piecemeal so as to prevent bleeding (fig 9). When the adenoma is separated from the bladder neck, it is pulled forward into the wound and cut from the pars membranacea urethra with the scalpel.

In some cases the entire procedure may be simplified if the adenoma is longitudinally divided into two halves, and a pair of forceps is substituted for the Young retractor, each half being then separately removed.

After the removal of the prostate, the inside of the bladder is cleansed and inspected. The urethral catheter is reinserted into the bladder along with a

rubber drainage tube,  $\frac{1}{2}$  inch (1.27 cm) in diameter (fig 10). The cut ends of the bladder neck and urethra may, when thought necessary, be drawn together with several catgut sutures. The wound is then packed with epinephrine gauze, the horizontal incision in the so-called capsule being sutured over a part of the tampon. The skin is then sutured, no attempt being made to unite muscle or fascia.

*Postoperative Care*—Immediately following the operation the bladder is irrigated with from 150 to 200 cc of warm salt solution. Thereafter, during the first twenty-four hours, this is repeated from every quarter to every half hour depending on the tendency to clot formation. The packing is loosened on the second day and removed on the third. The large rubber drain is removed on the

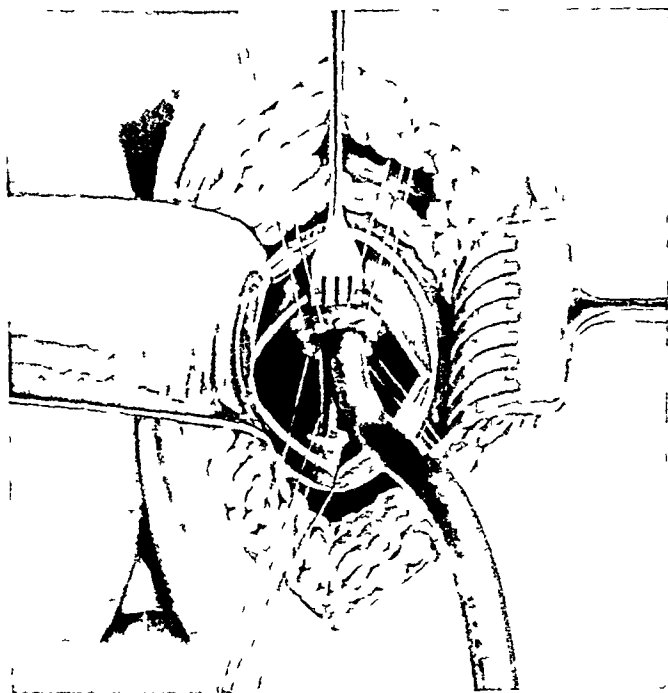


Fig 10—The prostate has been removed and the cut ends of the urethra and the bladder neck are being drawn together with several catgut sutures. A thick rubber tube drain lies in the bladder. The wound is now packed with gauze, the prostatic sheath being loosely sutured.

eighth to the tenth day and the urethral catheter is left in place for fourteen days except when encrustation demands earlier changing.

#### COMMENT

The present series includes 148 cases in which this method was used, with a mortality rate of 4.07 per cent. The age incidence was from 60 to 65 years, 38 per cent; from 65 to 70, 28 per cent; from 55 to 60, 22 per cent; from 70 to 75, 10 per cent; and from 75 to 80, 2 per cent.

This series includes the first cases in which this method was used, eight surgeons having operated, all of whom were performing the operation for the first time. Under these conditions, it seems only reasonable to think that the next series will show a decreased mortality.

#### SUMMARY

1 The Voelcke method of ischioirectal prostatectomy is presented

2 The advantages of this method are

(a) The operation is done entirely under the guidance of the eye

(b) Exact hemostasis by means of ligature, suture and packing is possible

(c) Because of exact visibility, the possibility of leaving small pieces of adenoma behind is unlikely

(d) Dependent drainage from the base of the wound is possible

(e) Death from operative shock has not been encountered

(f) Permanent fistulas or incontinence have not occurred

(g) Postoperative epididymitis can be almost entirely controlled by the performance of vasotomy before treatment with the indwelling catheter is inaugurated

(h) The series includes 148 cases in which the operation was performed by eight surgeons, with a mortality rate of 4.07 per cent

# CHOLEDOCHOGASTROSTOMY FOR SCAR TISSUE OBSTRUCTION OF THE COMMON DUCT\*

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Although a number of plastic operations have been done for injury to the common bile duct, a careful survey of the literature reveals that direct anastomosis of this duct with the stomach for relief of scar tissue obstruction has rarely been performed

Eliot,<sup>1</sup> in 1918, in his review of the literature on the surgery of the hepatic and common bile ducts, cited six cases in each of which an anastomosis was made between one of these ducts and the stomach. In only three was the anastomosis made between the common duct and the stomach. These three cases were those of Dujarier, O'Day and Brunner.

Dujarier's and O'Day's cases are reported in this article. Eliot stated that Brunner merely noted a successful case of choledochogastrostomy and gave no details.

Kehr,<sup>2</sup> in 1913, said that he had united the stomach to the hepatic duct in three cases but gave no details of the operation. Eliot cited one of Kehr's cases, in which the anastomosis was between the hepatic duct and the stomach.

Dujarier,<sup>3</sup> in 1911, reported the case of a woman, aged 50, on whom a cholecystectomy for gallstones had been performed. Symptoms persisted, including jaundice and fever. At the second operation, the common duct was found to terminate in a cul-de-sac, above which it was much dilated. The common duct was opened and explored with the finger. It showed no obstruction above the cul-de-sac. As the opening had been made near the stomach and there were adhesions between it and the duct, an anastomosis (lateral) was performed between the stomach and the duct. Two rows of fine silk sutures were used. The anastomosis was reenforced by a fold of omentum. The patient made a good recovery and remained well for three years after operation. No digestive disturbances resulted from the discharge of bile into the stomach.

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\* Submitted for publication, Nov. 12, 1929.

1 Eliot, E. The Repair and Reconstruction of the Hepatic and Common Bile Ducts, *Surg. Gynec. Obst.* **26** 81, 1918.

2 Kehr. Rückblick auf 2,000 operationen an den Gallenwegen, *Verhandl. d. deutsch. Gesellsch. f. Chir.* **42** 273, 1913.

3 Dujarier, C. Choledoco-gastrostomie chez une malade opérée antérieurement de cholecystectomie. *Bull. et mem. Soc. de chir. de Paris* **37** 1318, 1911.



In 1920, O'Day<sup>4</sup> reported a case in which an operation had been performed on the patient eleven years previously. This was reported by Eliot as a "personal communication" from O'Day. In this case the patient had repeated attacks of colic, followed by persistent jaundice. At operation, "a fistulous tract was found leading from the perforated duct to the lesser peritoneal cavity, which was shut off from the foramen of Winslow. In the lesser cavity was found a considerable amount of bile containing one calculus. During an attempt to fix the choledochus it broke off at a point just above the adherent mass in which the termination of the duct was embedded, and abundant bile exuded from the proximal end. An anastomosis was done between this stump and the anterior wall of the stomach in its lower one-third." Eleven years after operation, the patient was in excellent health, with no digestive disturbances. O'Day said that in this case, implantation of the stump of the duct into the stomach seemed the best and safest way out.

In 1927, Matthews<sup>5</sup> reported a case as a "choledochogastrostomy" in which symptoms had recurred after a cholecystectomy for gallstones. Jaundice was marked. At operation the hepatic duct was found greatly dilated and adherent to the duodenum, with a small opening into the duodenum. This fistula was closed. The opening into the hepatic duct was just at the junction of the right and left hepatic ducts. Bile and "sandlike stones" were found on exploration with the finger in each duct, and were removed. Then an anastomosis was made to the upper anterior surface of the stomach just proximal to the duodenum. The anastomosis was done by a suture method in two rows, much like gastro-intestinal anastomosis. This procedure in itself gives some idea as to the size of the dilated ducts. The patient made a good recovery, and has been well since the date of operation, July 28, 1924. (The anastomosis in this case was apparently between the hepatic duct and the stomach, although the designation of the operation would indicate that it was between the common duct and the stomach.)

Walters,<sup>6</sup> in 1929, reported seventeen operative cases of benign stricture of the common or hepatic duct. He said that he had found anastomosis of the common or hepatic duct to the duodenum the most satisfactory type of operation in such cases, provided that sufficient duct remains proximal to the stricture to permit anastomosis. In his tabulation of cases, he included two in which choledochogastrostomy was done. He did not describe the technic of this operation. In both

4 O'Day, J. C. *Surgery of Ductus Communis Choledochus*, *Ann Surg* **71** 293, 1920.

5 Matthews, A. A. *Choledcho-Gastrostomy*, *M Sentinel* **35** 152, 1927.

6 Walters, W. *Strictures of Common and Hepatic Bile Ducts*, *Surg Gynec Obst* **48** 305 (March) 1929.

cases cholecystectomy had been done elsewhere, but jaundice and pain had developed subsequently. In one case there was a stricture of the common and hepatic ducts and a stone in the hepatic duct. Choledocho-gastrostomy was done, and a T-tube was placed in the common duct. The immediate results were good and the tube was passed. Jaundice and fever, but no pain, recurred within a year. In the second case the patient died of intra-abdominal hemorrhage twelve hours after operation.

#### REPORT OF CASE

*History*—A woman, aged 48, was admitted to the Post-Graduate Hospital on June 25, 1929, with the complaint of jaundice, itching of the skin and pain in the epigastrium for the past few weeks, with increasing jaundice and itching.

The patient was operated on for abdominal tumor in 1919, for goiter in 1925 and for disease of the gallbladder in October, 1928. Otherwise the history was unimportant.

*Present Illness*—The patient dated her complaints to four weeks before examination, when she noticed that her skin was becoming yellow and that she had some discomfort in the epigastrium. There was no severe pain but an uncomfortable sensation in the upper part of the abdomen accompanied by belching without vomiting. Her condition gradually became worse. For the last ten days she had been bothered by itching of the entire body, as well as by increasing jaundice. She said that in October, 1928, she was operated on in Chicago for a condition of the gallbladder, after which there was drainage of bile until the early part of January, 1929. Then the wound healed, and she remained in fairly good health until about one month before admission to the hospital, when she began to have epigastric discomfort and jaundice, at that time she consulted her family physician who ordered that a series of roentgenograms of the gastro-intestinal tract be made; these were negative. The report from the previous operation was as follows: Operation revealed the stomach and the duodenum to be normal. The gallbladder was green and thickened. There were enlarged glands along the duct; no stones were palpated. Examination of the appendix showed adhesions around the cecum, with subacute inflammation. The uterus was normal in size and position. The adnexa showed adhesions. A cholecystectomy and an appendectomy were performed.

*Physical Examination*—The patient was thin and undernourished, with markedly jaundiced skin and sclera. She said that she was 20 pounds (9 Kg.) underweight. Her neck showed a scar from an operation for goiter but no evidence of thyroid enlargement. There was a firmly healed scar over the upper right rectus muscle and also a firmly healed lower midline incision. As a result of scratching, the patient had numerous abrasions over the arms, legs and body, with pruritus and

*Laboratory Data*—Urinalysis gave negative results. The bleeding time was four minutes, clotting began in five and one-half minutes and was complete in six minutes. The white blood count and the differential count were normal. The diagnosis was biliary obstruction from scar tissue.

The patient was given daily hypodermoclysis: 1000 cc. of 3 per cent dextrose and 15.5 grams (1 Gm.) of calcium chloride, intravenously, for four days.

At operation on July 3, 1929, the abdomen was opened through a right rectus incision, the previous scar being excised. When the peritoneum was opened



Fig 1—Dilated common and hepatic ducts A represents the site where incision was made in the stomach and the common duct

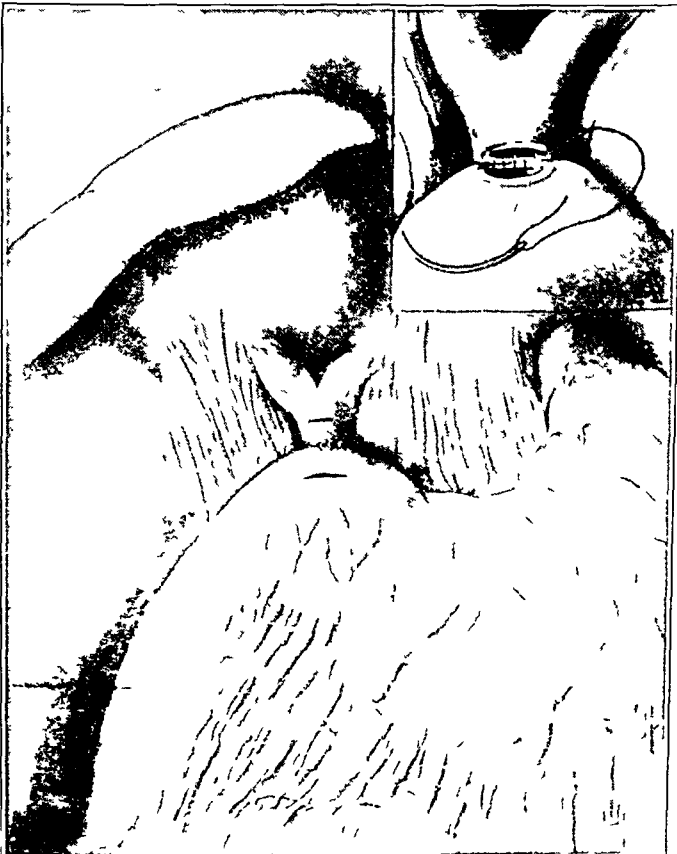


Fig 2—First row of sutures approximating the stomach to the common duct 1 shows a second row of posterior sutures, next the operator will continue the anterior row



Fig 3—The anterior row of sutures is completed, three mattress sutures are taken between the stomach and the liver



Fig. 4—The mattress sutures are tied approximating the stomach to the under surface of the liver

moderate adhesions were found in the right upper quadrant in the region of the gallbladder bed, but the gallbladder bed could be exposed without much difficulty, and the stomach was freely movable, the duodenum was adherent and definitely fixed. When the common duct was exposed a definite scar tissue obstruction was found 1 inch (2.54 cm.) below the hepatic veins, with a dilatation of the upper inch of the common duct and both hepatic veins. The common duct was opened, and the right and the left hepatic veins were probed and found to be patent (fig. 1). The common duct was definitely obstructed by scar tissue. The stomach could be easily approximated to the dilated portion of the common duct (fig. 2). It was impossible to approximate the duodenum to the common duct. A direct anastomosis between the common duct and the stomach was done, the steps of which were identical with the steps of a gastro-enterostomy. After completion of the anastomosis, three mattress sutures were taken from the stomach to the under surface of the liver to relieve any tension on the suture line between the common duct and the stomach (figs. 3 and 4). A small rubber tissue drain was inserted through the peritoneum. The abdomen was closed in anatomic layers.

*Postoperative Course*—The patient's convalescence was uneventful for the first few days. There was no leakage of bile around the drain until the fourth day, when the dressing was saturated with bile. On the fifth day, there was only slight leakage of bile on the dressing, and on the sixth day it entirely disappeared. The cigaret drain was removed on the sixth day, and from then on there was no leakage of bile. At this time, it was noticed that the jaundice was definitely subsiding and the itching diminishing. The patient continued to improve, and was discharged from the hospital on the twentieth day. At that time she was practically free from jaundice, and itching had entirely disappeared. The wound had healed, with the exception of a slight area at the lower angle which was infected.

The patient was last seen on Nov. 11, 1929, at which time she felt perfectly well and was free from jaundice. She had gained 18 pounds (8 Kg.) in weight since the operation.

#### COMMENT

The one reason for doing this operation was the ease with which the stomach could be approximated to the common duct for the anastomosis, without tension on the suture line.

125 East Seventy-Second Street

# THE REPAIR OF CLEFT PALATES AFTER UNSUCCESSFUL OPERATIONS

WITH SPECIAL REFERENCE TO CASES WITH AN EXTENSIVE LOSS  
OF PALATAL TISSUE

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If one is a young man and somewhat of a surgical optimist, a review of the measures used in operations on cleft palates is apt to temper one's enthusiasm somewhat and one may entertain a great many doubts as to the probability of surgical intervention ever attaining its ultimate goal—the ideal functional result—so far as the cleft palate is concerned. In the past many of the great minds in surgery as a glance at the names which represent the real milestones of progress will reveal have wrestled ardently with the problem of cleft palate.

In 1764, Le Monnier,<sup>1</sup> a French dentist reported the first successful repair of a cleft velum. Later, his success was followed by von Graefe<sup>2</sup> of Germany in 1817, Roux<sup>3</sup> of France in 1819 and Warren<sup>4</sup> of America in 1820. But it remained for Dieffenbach to report the first successful closure of both the hard and the soft palate in 1834. Baizeau<sup>5</sup> in 1853 and von Langenbeck<sup>6</sup> in 1861 claimed originality for the operation of Dieffenbach with its lateral incisions. But even today the operation bears the name of von Langenbeck.

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\* From the Surgical Department of the University of Kansas School of Medicine

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1 Le Monnier, quoted by Robert. *Memoires sur different objet de medicin* Paris Masson & Cie 1764 quoted by Verneuil. *A S S Memoires de chirurgie* Paris, Masson & Cie, 1877-1878, vol 1 p 506

2 Von Graefe C. *Die Gaumennaht ein neuentdecktes Mittel gegen angeborene Fehler der Sprache* J d Chir u Augenh **1** 556, 1820

3 Roux, P J. *Memoires sur la staphyloraphie* Arch gen de med **7** 516, 1825

4 Warren John C. *On an Operation for the Cure of Natural Fissure of the Soft Palate* Am J M Sc **3** 1 1828

5 Baizeau, quoted by Verneuil, A S S. *Memoires de chirurgie*, Paris Masson & Cie 1877-1878 vol 1 p 506

6 Von Langenbeck B. *Operation der angeborenen totalen Spaltung des harten Gaumens nach einer neuen Method* Deutsche Klinik **12** 231 1861 *Weitere Erfahrungen im Gebiete Uro-plastik mittelst Ablösung des mucosoperiostalen Gaumenerüberzuges* Arch f klin Chir **5** 1 1864

Feergusson has generally received credit for first advocating the severance of the palatal muscles (1845)<sup>7</sup> and also with osteotomy (1873)<sup>8</sup> of the horizontal processes of the palatal bones for relaxation. It appears, however, that Frohner<sup>9</sup> first carried out the former procedure in 1823, and Dieffenbach<sup>10</sup> the latter procedure in 1826. Billroth,<sup>11</sup> in 1861, made the suggestion that the hamular processes be fractured to relieve tension. The use of the mucosal flap from the septum to aid in the repair of the fissure was done first by Lannelongue<sup>12</sup> in 1877. The "criss-cross flap" operation of Davies-Colley<sup>13</sup> for closure of the hard palate appeared in 1890. In 1893, Brophy<sup>14</sup> suggested the wiring operation for bringing the separated alveolar ridges together at an early age. Finally, in 1902, the Lane<sup>15</sup> operation appeared which was an extension of the principle of the Davies-Colley flaps to both the hard and the soft palate.

#### THE USUAL OPERATIVE PROCEDURES

Practically all the common operations for the repair of complete cleft palates, such as the Lane, Warren and von Langenbeck, have a more or less common fundamental defect. When the palate is being repaired, the mucoperiosteal flaps have to be separated from the palate bones and brought down nearly to a horizontal level to obtain midline closure because the elevation of the horizontal plates of the palate bones on both sides are like the two sides of a raised drawbridge. Thus the upper surface of the freshly repaired hard palate is raw, and as granulation occurs the soft tissues of the hard palate either come up to the horizontal plates or the plates go down to the soft tissues. Probably

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7 Fergusson, William. Observations on Cleft Palate and on Staphyloraphie. *Tr Med Soc-Chir* **28** 273, 1845, On Cleft Palate and on Staphyloraphie, *Med Times* **16** 25, 1847, On Hare-Lip and Split Palate, *Lancet* **1** 719, 1864.

8 Fergusson, William. A New Operation for Cleft Palate, *Lancet* **11** 784, 1873, Successful Treatment of Four Cases of Cleft in the Hard Palate by a New Operation, *ibid* **1** 298, 1874.

9 Frohner. "Nottizen" chirurgische Kupfertafel, Weinmer, 1823.

10 Dieffenbach, J. F. Chirurgie Erfahrung, 1834, no 324, p 168, *Die Operative Chirurgie*, Leipzig, F. A. Brockhaus, 1845.

11 Billroth, T. Ueber Uranoplastik, *Wien klin Wchnschr* **2** 241, 1889.

12 Lannelongue. De l'uranoplastie osteo-muqueuse, *Bull et mem Soc de chir de Par* **111** 467, 1877.

13 Davies-Colley, T. N. C. On a Method of Closing Cleft of the Hard Palate by Operation, *Brit M J* **11** 950, 1890.

14 Brophy, T. W. Brophy's Operation for Cleft Palate, in *Catching Comp Pract Dent Atlanta*, 1894, vol 258, p 262, *Proc Thrd Internat Dent Cong* **152** 153, 1900, quoted by Stone, in Bryant and Buck. *American Practice of Surgery*, New York, William Wood & Company, 1908, from Park. *Surgery*, Philadelphia, Lea Brothers & Company, 1893.

15 Lane, W. A. On Cleft Palate, *Lancet* **11** 433, 1902.

both movements occur to some extent, especially in the young, but the tendency for the anterior end of the soft palate to be pulled up to the apex of the V formed by the posterior edges of the horizontal plates of the palate bones is always present

The observance of a few cases of narrow recessive deformity of the upper jaw in the adolescent who has undergone an operation in infancy in whom the alveolar ridges were wired together warns one to let the maxillary bones alone if possible. Thus the Brophy wiring operation, which necessitates a later operation of the Warren type, is losing adherents. When the surgeons who still adhere to the belief that the early wiring together of the alveolar ridges is a good procedure are excluded, opinion is fairly uniform as to the operative methods to be used and to the necessary essentials preceding closure of the cleft palate in which sufficient tissue is present. In selected cases the Lane operation may be useful, yet because of the likelihood of a slough of the upper flap and the probability that the cicatrix will interfere with mobility of the velum, it is not generally popular. The Warren operation without the lateral incisions gives good results in palates with high vaults and in palates in which the arch of the alveolar ridge has been narrowed by a wiring operation. The von Langenbeck operation with its lateral relaxing incisions, loosening of the raphe at the posterior end of the palatal bones and the preservation of the posterior palatine artery to each flap seems to have withstood the test of time for the routine case and probably is justly the most popular operation for the usual cleft palate.

#### PALATE LENGTH NECESSARY

Aside from its function of forming a diaphragm between the nasopharynx and oropharynx in the act of swallowing, the palate normally should be able to form a "flap valve" between the resonating cavities of the nose and the mouth at the moment of the proper articulation of a great many of the consonants—all except m, n and ng. In "cleft palate" speech some of the air which in the articulation of nearly all consonants ought to be expelled through the mouth escapes through the cleft into the nose, where it vibrates in the nasal cavity and finally escapes through the anterior nares. The oral consonants are converted into the voiced nasal consonants and cannot be voiced as loudly, as clearly or as forcibly as they should be.

Thus one of the outstanding needs in surgical intervention of the cleft palate today is a workable procedure which effectually lengthens the soft palate. With this hypothesis in mind a few clinical experiments were performed on badly damaged palates with the hope that the way to some improvement of the present-day results might become somewhat clearer. The hope was entertained that these badly damaged palates might show sufficient functional improvement after operation to



warrant the extension of the same methods to the ordinary case of cleft palate in which operation was not performed or the case in which operation had been done with failure to obtain midline union in which no tissue loss had occurred. As yet, however, the justification for such an extension of the type of operations to be described has seemed questionable.

#### THE SEVERELY DAMAGED PALATE

Besides patients with the ordinary types of cleft palate in which operations were not performed or the cases in which operations were performed with failure to obtain midline union but in which no tissue loss has occurred, a number of patients present themselves for repair who have been operated on one or more times previously and in whom there is unmistakable evidence of an old slough. An occasional patient is also seen who shows a marked disuse atrophy of the soft palate which was due to the fact that an operation was not performed at the proper time.

To show the interrelation and to aid in discussion the severely damaged palates have been divided into three groups, as follows:

- 1 Cases in which midline union is probable or has occurred but in which the velum is markedly atrophic or definitely shortened by cicatrix.
- 2 Cases in which after operation the tissue of the hard palate is preserved so that the closure of the hard palate has been obtained or is obtainable, but in whom a considerable part of the velum has been lost.
- 3 Cases in which a previous operation has resulted in a sloughing of so much of the tissue of the hard palate and of the soft palate that repair is obviously impossible without the use of tissue from other sources than the mouth.

The obvious need in the palates of the first group is the addition of tissue without interference with mobility so that the velum can come in contact with the posterior pharyngeal wall. In palates of the second and third groups, any soft tissue diaphragm built in to take the place of the soft palate or the whole palate, respectively, which does not obstruct breathing ought to be an aid in closing off the nasopharynx from the oropharynx in the act of articulation.

Most of the patients selected were of the type for whom the usual methods of operation had little to offer. In each case the procedures used for repair it seemed reasonable to believe, would replace the palatal tissue loss. The results obtained thereby are presented by brief histories of the cases.

#### REPORT OF CASES

The report of the case that follows represents an effort to solve by operation the problem of the patient with an almost complete loss of the velum (group 2). It was obviously impossible to repair such a palate without tissue other than that from the palate.

CASE 1—On Nov 21, 1926, a woman aged 21 was admitted to the Bell Memorial Hospital with the history of four unsuccessful operations on the palate.

From a point opposite the level of the larynx a long pedicled flap of mucosa, about 6 cm in length by 3 cm in width, was dissected upward off the posterior pharyngeal wall in the midline so that the base of the flap was about on a level with the posterior edge of the palate. The flap could then be pulled forward to the posterior edge of the hard palate. From the remnants of the upper surface of the soft palate a semicircular flap was loosened with a right angled knife and turned downward and toward the midline so that the mucosal covering was adjacent to the tongue. This procedure left a large raw area on the upper surface of the remnants of the velum. The pharyngeal flap was then sewed into this raw defect. Thus a mucosal covering was made for the upper surface of the soft palate. The flaps from the remnants of the soft palate then were drawn to the midline beneath the pharyngeal flap and the edges were sewed together (figs 1 2 and 3).

On the day following the operation it was noticed, to my great surprise, that the patient articulated her words nearly perfectly. Her

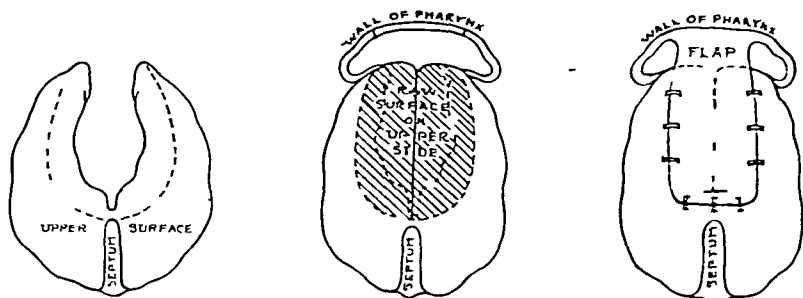


Fig 1 (case 1)—Diagram of the upper surface of the soft palate, showing method in which the "shelf" flaps were turned medialward and the position of the pharyngeal flap after it was thrown into the raw area on the upper surface of the palate.

speech was improved so startlingly that prematurely the conclusion was reached that the key to the problem of defective speech in cleft palate had been found. But as the flap from the pharyngeal wall gradually tubed itself, although the freedom of the airway improved her speech was somewhat less perfect. This patient has been followed up for two and a half years. When she has a cold she has some respiratory difficulty because of accumulated discharge in the nasopharynx especially at night. Her speech is a little thick and reminds one of speech when the mouth is too full of food but the cleft palate type of speech has been remedied. The improvement in the articulation of her words is really remarkable (fig 4).

In case 2 an attempt was made to improve speech by lengthening the short atrophic velum. This soft palate was typical of the type seen in which operation is postponed until adult life (group 1). A fairly



Fig 2—Lateral midsection view of the palate, pharynx and pharyngeal flap after it was sewed on the upper surface of the soft palate as in case 1

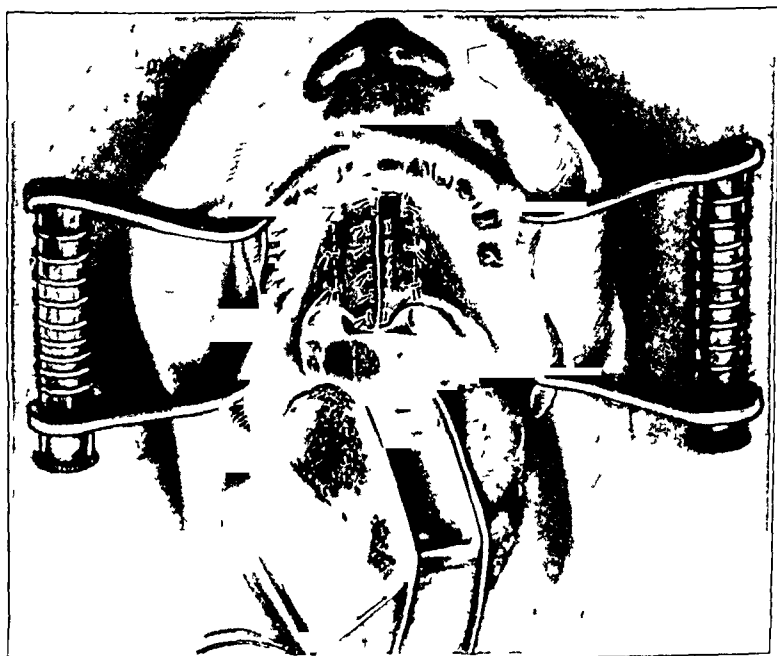


Fig 3—The appearance of the soft palate from inside the mouth after the pharyngeal flap was sewed to the upper surface of the soft palate as in case 1 (In cases 2 3 and 4 the methods of turning the flaps were reversed because the latter operation is easier to perform mechanically)

marked disuse muscle atrophy of the velum was present, but there was sufficient palatal tissue to come together in the midline

CASE 2—On Dec 19, 1928, a man aged 23, entered the Bell Memorial Hospital with a complete cleft of the velum. A pharyngeal flap was turned downward instead of upward and thus the flap was attached on the under surface of the new velum instead of on the upper surface as in the preceding case. The method of placing the flap in this case was reversed, because technically it is easier to raise the semicircular shelf of flap on the soft palate from the mouth side than from the nasal side (figs 5 and 6)

Six weeks later, the pharyngeal flap was detached from the posterior pharyngeal wall. The tail of the flap was cut rather long so that it could be turned over on the upper surface of the velum and doubled on itself to make a thick mass of tissue as wide and as long as possible



Fig 4 (case 1)—Photograph of the inside of the mouth, taken on July 5 1929

This patient has been followed up for about eighteen months. He is an intelligent person and practices speaking consonants daily with the aid of his wife, who detects changes in sound better than he. Improvement in the articulation of his words is definite.

Following the operations in the first two cases, in February, 1927, a case was reported by Kirkham<sup>16</sup> in which he sutured together the superior constrictor muscle of the pharynx at the sides of the pharyngeal cavity. Speech was nearly normal during the three days that the stitches held. Kirkham was led to believe that the shortening of the loop of the superior constrictor muscle was significant and had more of a bearing on correct articulation than heretofore had been thought

<sup>16</sup> Kirkham H. L. D. Preliminary Paper on Improvement of Speech in Cleft Palate Cases. *Surg. Gynec. Obst.* 44:244, 1928.

Passavant<sup>17</sup> long ago called attention to the hypertrophy of the superior constrictor muscles of the pharynx in the patient with cleft palate. Overdevelopment of the superior constrictor muscle is explained on the basis of its being the only muscle in articulation utilized by the patient with cleft palate to close off the nasopharynx from the oropharynx.

It seems reasonable to attribute some of the improvement in speech experienced by the patient in case 1 to a tendency of the superior constrictor loop of muscle to be pulled forward somewhat by the flap which connects the velum with the posterior pharyngeal wall. More significant than the tendency of the forward pull, however, and applicable whether the pharyngeal pedicle flap is severed or not, is the narrowing of the pharynx obtained because of the removal of the central mucosal strip.

The third case is an example of rather marked cicatricial contracture of the soft palate with some muscle atrophy (group 1). The hard palate was closed completely except for a small hole in the midline. The velum was separated to within about 1 cm. of the hard palate, was badly scarred and was shortened, and some of it appeared to be missing.

CASE 3—This patient was  $2\frac{1}{2}$  years old when first seen in Bell Memorial Hospital. Two operations had been performed previously. He was operated on on Jan. 16, 1928. The velum was rebuilt by the utilization of a pedicled flap from the posterior pharyngeal wall. The pharyngeal flap was turned downward and placed beneath the raw surface formed by the turned up flaps from the soft palate, as in case 2 (figs. 5 and 6).

This boy's speech shows improvement, however, he is apparently subnormal mentally, and it is difficult to judge accurately the amount of improvement. He has been followed up for eighteen months. His mother thinks that the improvement in speech has been definite. The pedicled flap still remains attached to the pharyngeal wall.

The patient in case 4 had suffered from about as much loss of the tissue of the soft palate as the one in case 1, and falls in group 2 of my classification.

CASE 4—This patient was operated on on Aug. 28, 1928, in Bell Memorial Hospital, when  $3\frac{1}{2}$  years of age. He had had three previous attempts at closure of the palate. More than one half of the soft palate had sloughed. The hard palate, however, was closed. A shelf of mucosa from the remnants of the soft palate was turned upward with the mucosal surface toward the nasal cavity. By swinging a flap from the posterior pharyngeal wall with the pedicle downward to the raw surface of the upturned flaps from the soft palate, a new soft palate of good length and width was constructed, as in cases 2 and 3 (figs. 5 and 6).

17 Passavant G. Ueber die Beseitigung der naselnden Sprache bei angeborenen Spalten des harten und weichen Gaumens, *Arch. f. klin. Chir.* 6:333, 1865.



Fig 5—Medial cross-section view of the method used when the pharyngeal flap is turned downward (In cases 2, 3 and 4 the methods of turning the flaps were reversed, as shown in figures 5 and 6 because the procedure is easier to perform mechanically )

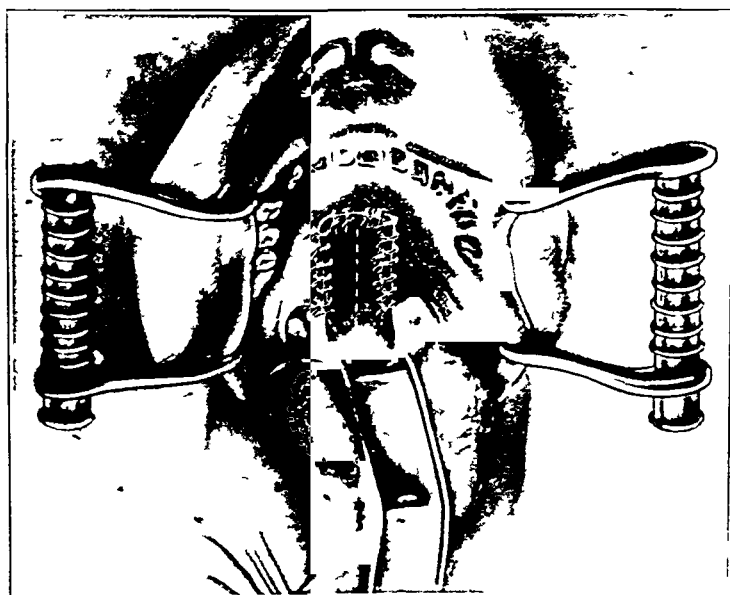


Fig 6—View of the palate from within the mouth when the pharyngeal flap is turned downward instead of upward

Improved articulation in this patient was immediate and fairly marked. He has been observed for ten months. The pharyngeal flap has not been detached from the pharyngeal wall.

#### PREVIOUS IDEAS ON PALATE LENGTHENING

In 1876, Schoenborn<sup>18</sup> advocated the use of a flap from the posterior pharyngeal wall. In 1878, Passavant tied the uvula to the posterior pharyngeal wall by turning small flaps so that raw surface would be to raw surface. The idea was not accepted with enthusiasm, although it was admitted that speech was improved. Sedillot<sup>19</sup> criticized the idea on the basis that surgeons had known that in cases of stricture between the nasal and buccal cavities the nasal type of speech remained. Again, recently, Rosenthal<sup>20</sup> utilized a flap from the posterior pharyngeal wall to repair the velum. Von Kuster's<sup>21</sup> lengthening operation by means of a portion of the detached edge of the cleft also belongs to this group.

In 1922, Blair<sup>22</sup> performed an operation in which flaps from the cheek were outlined and turned in through the lateral incisions on the upper raw surface of the palate anterior to the upper mucosal surface of the velum to increase the mucosal covering of the upper surface of the palate. This operation lengthens the upper surface of the palate and probably allows the velum to drop down a little.

In 1925, Dorrance<sup>23</sup> described an operation for the lengthening of a palate in which the soft tissue of the hard palate and the raphe of the soft palate are loosened from the horizontal plates of the palatal bones. An encircling incision was made within the alveolar margins and both the hard and the soft palates were displaced backwards. Again, Limberg,<sup>24</sup> in 1927, and Lvoff,<sup>25</sup> in 1928, presented somewhat similar methods. In these operations, even if the flaps of the hard palate did retain their blood supply, it would seem probable that the raw surface

18 Schoenborn. Ueber eine neue Methode de Staphylorrhaphie, *Arch f klin Chir* **19** 528, 1876.

19 Sedillot, C., quoted by Christopher Heath, in John Ashhurst. *The International Encyclopedia of Surgery*, New York, William Wood & Company, 1889, vol 4, p 911.

20 Rosenthal, W. Pathologie und Therapie der Gaumendefekte, *Fortschr Zahnh* **4** 1021, 1928.

21 Von Kuster. Den Operation der complizierten Nasenscharte, *Zentralbl f Chir* **32** 713, 1905, Ueber die Operative Behandlung der Gaumenspalten, *Arch f klin Chir* **46** 215, 1893.

22 Blair, V. P. Personal communication to the author.

23 Dorrance, George M. Lengthening of the Soft Palate in Cleft Palate Operations, *Ann Surg* **82** 208, 1925.

24 Limberg, A. Innovations in Operative Methods, *Zentralbl f Chir* **54** 1745 1927.

25 Lvoff, P. P. Operation for Lengthening Palate. *Vestnik Khir* **13** 212, 1928.

between the upper mucosal surface of the velum and the posterior edge of the horizontal plates of the palate bones would simply scar and pull the soft palate back to its former position

In one of my recent cases (1929) the upper surface of the junction of the hard and soft palates was relined with cheek flaps, as in the operation of Blain, to obtain length of the upper surface of the palate, and the whole palate was pushed back, as in Limberg's operation, to obtain length of the lower surface. This operation appears logical

#### NEARLY COMPLETE LOSS OF PALATAL TISSUE (GROUP 3)

In persons in whom only remnants of both the hard and the soft palates remain after operations in which a slough has occurred, a substitute for palatal tissue can be built from tubed pedicled flaps from either the neck or the arm. The paramount question is whether or not a complete new palate built in with inert tissue is of enough functional value to compensate the patient for his trials during a tedious operative procedure

The brief abstracts of the three cases that follow outline the methods by which such difficult palates can be repaired and give some evidence of the difficulties to be overcome. These cases fall in group 3 of the classification

In case 5 the young woman had had several previous operations due to which at least one half of the tissue of the hard palate was absent and practically all of the tissue of the soft palate had sloughed. The tissue loss in this case seemed too great to allow a successful repair by the method of a posterior pharyngeal flap alone. It was decided to use a tubed pedicled flap from the left arm

CASE 5—A girl, aged 17, was admitted to the Trinity Lutheran Hospital on July 15, 1928. On July 16, the flap was raised from the arm and tubed. On the under surface of the upper end of the flap, which was the part to go into the mouth, a full thickness skin graft was applied. A full thickness skin graft was sewed into the defect on the arm left after the flap was raised. About a week later the upper end of the flap was detached.

On July 28, the flap was sewed in the defect of the palate after shell flaps were turned upward from remnants of the old palate. A flap was also raised from the posterior pharyngeal wall and sewed to the upper surface of the distal end of the flap that had just been placed in the mouth. A block was wired between the teeth to prevent her from biting the flap and a cast was applied to the head and arm to hold them in proper position. Twelve days later the pedicle of the flap was cut across and the cast removed. One week later, the proximal end of the flap in the mouth was smoothed out and united to the anterior hard palate (figs 7, 8, 9, 10 and 11).

The girl was intelligent. She had led her class in high school but because of the defect in speech caused by the palate she attempted to get along in the world by saying only "yes" and "no," smiling and shaking



her head. After the palate was repaired she began to try to talk, and although articulation was imperfect she did show improvement. She is now diligently attempting to overcome her defect in speech by self-training.

When this patient's palate was examined on July 15, 1929, to my surprise it was noted that the new palate contracted and moved. The tissue in the midline, although incapable of movement itself, had evi-



Fig. 7—The flap one week after it was raised from the arm. At the upper end and on the under surface a full thickness skin graft was grown. (This is not visible, however.) Beneath the gauze a full thickness skin graft, which is not visible because of gauze, was sewed into the defect caused by the removal of the flap.

dently been rendered taut by the attachment of the remnants of the palatal muscles at the sides so that when the muscles contracted the whole soft palate showed movement. At this time her speech was remarkably improved. The posterior tip of the new palate was still attached in the midline to the posterior pharyngeal wall. This will be detached at a later date so that the effect on speech can be observed.

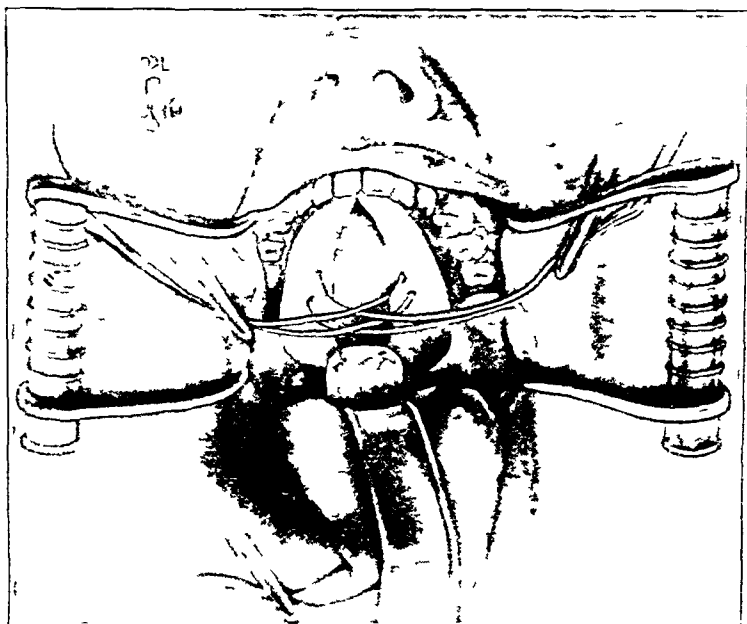


Fig 8—The methods of turning the shelt-flaps from the sides of the palatal tissues and from the posterior pharyngeal wall. The flap from the arm is then sewed well back into the mouth and put in contact with the raw surfaces.



Fig 9 (case 5)—The inside of the mouth after the operation was finished. Note that the pharyngeal flap is sewed to the tail of the skin flap from the arm and the 'shelt' flaps of mucosa have been turned upward above the skin flap from remnants of tissue at the side of the palate.

The patient in case 6 had had several previous operations on the palate and practically all of the palate had sloughed. Because of the discomfort of an arm cast, I chose to use a flap from the neck. His alveolar ridge was cleft, so I planned to grow the flap to the lip so that the end



Fig 10 (case 5)—A photograph of the plaster cast and flap as thrown into the mouth from the arm



Fig 11 (case 5)—Appearance of patient a few months after operation

beneath the chin could be detached and passed through the cleft. Thus the discomfort of a mechanism to keep his mouth open would not be necessary.

CASE 6—A boy, aged 2 years was admitted to Bell Memorial Hospital on Nov 15, 1928. A flap was raised from the neck and wall of the upper part of the chest with its base beneath the chin. Twelve days later the distal end of the flap was turned upward and attached beneath the upper lip. Thus a "jump flap" was made of it. About this time the patient developed influenza and ran a fever for about a week. It was suggested to his mother that she take him home at this time. However, as she was somewhat sensitive about his appearance, he was kept at the hospital. He should have gone home at this time for a long rest and complete recovery. On Feb 8 1929 the "jump flap" with its pedicle beneath the upper lip was turned into the mouth through the cleft alveolar ridge. The flap grew perfectly, but considerable trouble was experienced in getting the child to eat. He had practically a normal temperature after the first two or three days following the operation. Laboratory observations were negative except for a hemoglobin of 50 per cent. A transfusion was given, after



Fig 12 (case 6)—Appearance of patient after the flap had been raised from the neck.

which he began to eat a little and sit up in bed. On the evening of February 20, twelve days after operation, the nurse took him in her arms and gave him a feeding, after which she left the ward. She returned in about fifteen minutes and he was dead. No autopsy could be obtained.

The exact cause of the boy's death remains uncertain, but a lesson should be learned. He should have been given two or three months' rest to improve his condition before the flap was placed in the mouth. Perhaps it might have been better judgment to have postponed the operation until the child was several years older (figs 12, 13 and 14).

The patient in case 7 was 21 and had undergone several operations on the palate in babyhood after which the hard and soft palates had sloughed almost completely.



Fig 13 (case 6) —A drawing of the flap after it had been attached beneath the upper lip and its raw surface had been grafted by the Thiersch graft



Fig 14 (case 6) —A drawing of the 'jump' flap after it had been severed from the neck and turned in to build the new palate. Note the side "shell" flaps and the posterior pharyngeal flap turned on the upper surface of the skin flap

CASE 7—On June 17 1929 in Trinity Lutheran Hospital a flap was raised from the left arm and tubed. On July 2, the flap was placed in the mouth in a manner similar to that used in case 5. On the second night after operation a tracheotomy was done because of laryngeal edema.

For a few days following the tracheotomy he had a temperature of 103.5 F which gradually subsided. After two weeks the flap was cut next to the arm.



Fig. 15 (case 7)—Appearance of patient after the flap had been sewed into the mouth. The patient's mouth is held open by a triangular edge of wood which is wired between the teeth.



Fig. 16 (case 7)—As much of the new palate as could be shown by a photograph, two months after operation.

and the plaster fixation was removed. Two days after this he was sent home for two weeks. After this time he reentered the hospital to have the anterior end of the flap smoothed out and attached within the alveolar curve. He left the hospital five days later (figs. 15 and 16).

It is possible that a tracheotomy should be a part of this operation, unless an experienced nurse is in constant attendance. If a tracheotomy is not made at the time of the original operation, the instruments necessary to do a tracheotomy should be kept at the bedside for the first few days. At the present time (Sept 20, 1929) this patient is at work and his speech is nearly normal. The nasal tone has disappeared from his speech. The posterior part of his palate moves slightly when he swallows or speaks. The flap is still attached to the posterior pharyngeal wall in the midline.

#### PREVIOUS USE OF PEDICLED SKIN FLAP

The idea of the repair of a palatal defect by a flap from elsewhere than inside the mouth is rather ancient. It was first unsuccessfully attempted by Blasius<sup>26</sup> by the use of a flap from the neck. Thiersch,<sup>27</sup> in 1867, and Rotter,<sup>28</sup> in 1869, used the principle successfully. Later the method was successfully used by von Eiselberg<sup>29</sup> and Blair.<sup>30</sup>

#### SUMMARY

By the use of a pedicled flap from the posterior pharyngeal wall a method is presented which will lengthen somewhat the short velum without narrowing the nasopharynx or oropharynx sufficiently to interfere with the function of breathing or swallowing. The lengthening of the velum and the narrowing of the oropharynx obtained have improved speech and aided particularly in the articulation of the oral consonants in the persons so far observed. A pedicled flap from the posterior pharyngeal wall can be used in the successful reconstruction of a diaphragm of tissue between the nasopharynx and the oropharynx and is particularly applicable to those cases in which a considerable part of the velum has sloughed. In the past, such persons have usually been advised that surgical intervention has nothing to offer. The results reported definitely contradict the truth of such a hopeless verdict. The functional results in this group (group 2) are particularly satisfactory and hopeful. It is possible to use the pedicled flap from outside the mouth to repair this type of palate, but the procedure necessitates several operations and is far more difficult for both the patient and the surgeon.

26 Blasius, quoted by von Eiselberg, Frederick. *Zur Technik der Uranoplastik*, Arch f klin Chir **64** 509, 1901.

27 Thiersch, C. Verschluss eines Loches im harten Gaumen durch die weichtheile der Wange, Arch f d Heilkunde **9** 159, 1868.

28 Rotter, Julius. Deckung eines Defectes im harten Gaumen mittelst eines Sternlappens, Munchen med Wchnschr **36** 535, 1889, *Plastische Operation an der Mundhöhle und in der Nase*, Verhandl d deutsch Gesellsch f Chir, 1889.

29 Von Eiselberg, F. *Zur Technik der Uranoplastik*, Arch f klin Chir **64** 509, 1901.

30 Blair, V. P. Operative Treatment of Difficult Cases of Palate Defects After Infancy, Surg Gynec Obst **12** 289, 1911.

For the repair of the palate in which most of the tissues of both the hard and the soft palate have sloughed (group 3), a pedicled flap of skin and subcutaneous tissue from the arm or neck can be used. Obviously sufficient tissue to repair this extensive defect must be obtained elsewhere than from inside the mouth. Although the tediousness of this procedure is admitted the results in the preceding cases indicate that a diaphragm of skin and subcutaneous tissue is better than no palate or an obturator and is distinctly worth while. The movement of the new palate obtained after transplantation of a flap from the arm (cases 5 and 7) gives proof of the ability of the remnants of the palatal muscles which are attached at the sides of the new palate to move the central flap somewhat. The amount of this movement will probably depend on the amount of good muscle available for insertion at the sides. Thus the principle of the application of a pedicled flap from outside the mouth to repair a gross loss of palatal tissue places at the surgeon's command a final method, by the use of which, it can be said with truth, a defect of the cleft palate does not exist in which surgical intervention has nothing to offer, provided enough tissue remains within the alveolar curve to serve as a raw base of sufficient width to obtain union after the skin flap is sutured in place.

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#### ABSTRACT OF DISCUSSION

DR. FREDERICK A. FIGI, Rochester, Minn. I believe that the ingenious procedure which Dr. Padgett has presented for taking care of some of the difficult postoperative cleft palates, that is, the use of a flap from the posterior pharyngeal wall, is a real contribution. This should prove of decided value in taking care of some of the bad postoperative cases. At the Mayo Clinic, in the ordinary run of primary cases of cleft palate, our routine procedure has been the von Langenbeck operation to which he referred. Those patients presenting unusually wide defects, whether primary or due to postoperative loss, are taken care of with the two-stage delayed flap operation described by New in 1922. This consists of elevating the soft tissues on either side of the defect by means of a long lateral incision just inside the alveolar border. The double pedicled flap thus formed is crowded toward the midline by means of an iodoform gauze pack on either side. After from five days to a week the margins of these flaps are pared and sutured. In cases presenting still wider defects, an attempt is made to close the hard palate only in this manner at the first series of operations, the soft palate being closed by a similar two-stage procedure after several months. The length of the lateral incisions does not appear to have a direct bearing on subsequent palatal function, even in those cases in which the incisions are extended laterally around the tuberosity and well back into the commissure. Transforming the tensor palati into a levator by breaking off the hamular process of the external pterygoid plate, as suggested by Dorance and others, also at times assists in securing relaxation without subsequent interference with function. Multiple stage operations must of course be attended by the production of a greater amount of scar tissue and thereby increased rigidity of the palate. However, we have seen no appreciable difference in the function of palates closed in this manner in comparison with those in which we have secured primary union.



This multiple stage operation will permit of closure of many of the bad post-operative cases in which primary closure is entirely out of the question. I believe that this should be tried in preference to the use of a flap from the posterior wall if it appears at all advisable, for a closure obtained in this way will give an incomparably better functioning palate than one into which inert tissue has been introduced. Personally, I cannot become enthusiastic over the use of cutaneous flaps for the closure of wide palatal defects, even though the case may be hopelessly inoperable otherwise. The advantage of the introduction of this inert mass of tissue into the palate appears questionable to me in view of the difficulties associated with the operation and the hazards involved in comparison with the ease of closing such a defect satisfactorily with an artificial velum.

# CYSTIC CIRRHOSIS OF THE BREAST \*

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The occurrence of cysts in the female breast is common. Some of these cysts develop apparently from distended lactiferous ducts (galactoceles). They are comparatively unimportant and are not puzzling from either a morphologic or a clinical point of view. The presence of multiple often small cysts in the gland tissue proper of the breast is of far greater importance. The interpretation of their nature and histogenesis has been studied by a great number of authors yet no consensus has been arrived at. This is demonstrated sufficiently by the large number of names given to this condition. The confusing nomenclature includes, among others, the following terms: polycystic breast, cystic disease, polycystoma, hydrocystoma, cystic epithelioma and epitheliofibrosis of the breast.

The main questions that arise in studying this condition concern the histogenesis of the cysts, the nature of their matrix, the character of the epithelial proliferation and its relationship to neoplastic conditions and, finally, the part played by the stroma in the development of the process.

A short survey of the literature will show the divergence of opinion concerning these questions.

## REVIEW OF THE LITERATURE

Astley, Cooper and Langhans<sup>1</sup> were among the first to study cystic disease of the breast, but the first extensive studies of this subject were those of Reclus<sup>2</sup> (1865-1888) who described the disease as "maladie cystique des mamelles". His examinations were so important particularly from a clinical point of view, that later writers referred to this disease as "maladie de Reclus". His description and that of all the later authors agree in one point that there is an abundance of connective tissue in the breast with hyalinization of the fibers and a varying amount of spindle and round cells in between. With the

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From the Department of Laboratories, United Israel Zion Hospital

1 Langhans. Virchows Arch f path Anat 58 137 1873

2 Reclus. Rev de chir 1865 p 761. Clin chir de la Pitie 1883. Gaz d hop 1887 no 83. Rev de chir 1888 p 248

increase of this fibrosis, the lobules become more and more separated and the glandular parenchyma more and more scattered. Compression of the epithelial elements by the fibrous tissue is often predominant, the compressed glandular acini are often cut off from their lactiferous duct (Hertz, Ingier,<sup>3</sup> Langhans, Samelson)

While the importance of fibrosis is universally accepted, its pathogenesis has been attributed to various causes. The first author who suggested its development from an inflammatory process was König<sup>4</sup> (1880), who referred to the condition as "mastitis chronica cystica". In France, Trelat and Trillaux<sup>5</sup> brought forth a similar conception, while Phocas and Quenu<sup>6</sup> compared the mammary lesion with the cirrhosis of the liver or the kidneys which they also believed to be of inflammatory origin. They coined the name "cirrhose epithéliale mammaire".

Those who advocated the inflammatory theory relied on the presence of round cell infiltration, the cellularity of the connective tissue in the earlier stages and occasionally on the abundant presence of leukocytes. The changes of the epithelial tissue elements were considered merely as secondary to the inflammatory process and were compared to similar lesions in other glandular organs subjected to chronic inflammation (Haeckel, Maly, Glannan,<sup>7</sup> Rohloff,<sup>8</sup> Lichtenhahn<sup>9</sup>). Other authors who believed in the inflammatory conception, such as Borst, Cornil<sup>10</sup> and Delbet,<sup>11</sup> stressed the diffuse nature and the frequently bilateral occurrence of the condition, its occasional combination with adenomatous growth and the early participation of the epithelium in the proliferation.

Even those authors who believed in the inflammatory character of the disease and held that the process starts primarily in the connective tissue had to admit the striking character of the epithelial changes. The development of multiple and often large cysts with metaplasia and finally stratification of the epithelium and of active proliferation with abundant mitoses was so suggestive that many investigators felt inclined to class these changes with neoplastic processes.

While Reclus, Langhans and others explained the cysts by mechanical distention of the acini, Brissaud assumed that active proliferation of the epithelium was the cause of cyst formation and classified the

3 Ingier. *Virchows Arch f path Anat* **198** 338, 1909

4 König. *Zentralbl f Chir*, 1893, vol 3

5 Trelat and Trillaux. *Rev de chir*, 1888

6 Phocas and Quenu. *Rev de chir*, 1888

7 Glannan. *South M J* **2** 806, 1909

8 Rohloff. *Deutsche Ztschr f Chir* **54** 106, 1900

9 Lichtenhahn. *Deutsche Ztschr f Chir* **90** 507, 1907

10 Cornil. *Tumeurs du sein*, Paris, 1908

11 Delbet. *Traité de chirurgie de I c Dentu et Delbet*, 1899 vol 7

disease as a neoplasm ('epitheliome cystique intra-acineux') Sicre<sup>12</sup> shared his opinion and was the first to emphasize that, although cystic disease of the breast is a benign tumor it is noteworthy for its potentiality to malignant degeneration. The neoplastic conception was stressed particularly by Schimmelbusch who claimed that the essence of the process was the proliferation of the epithelium which fills up the acini and is followed by disintegration in the center, thus forming cysts. Production of connective tissue between the lobules of the breast gland is only secondary and of no real importance. The condition based on active epithelial proliferation and characterized by formation of cysts would justify the name of cystadenoma of the breast. A large number of later investigators accepted Schimmelbusch's<sup>13</sup> point of view (Keibel,<sup>14</sup> Saar,<sup>15</sup> Tietze,<sup>16</sup> Goens,<sup>17</sup> Hahn,<sup>18</sup> Silveira). Most of these authors stressed the intensity of the epithelial proliferation which often goes beyond simple hyperplastic or even adenomatous conditions and would justify the assumption that they already belong to precancerous changes.

An intermediary position was taken by Askanazy,<sup>19</sup> who emphasized the importance of the fibrosis and held that the connective tissue also participates in the process of proliferation. He recommended the name "epitheliofibrosis cystica." Other authors, such as Sasse suggested the possibility that both neoplastic and inflammatory changes concur in the development of the cystic disease.

To summarize briefly those who believe that the disease is of inflammatory origin base their contention on the following arguments: the presence of round cell infiltration, leukocytes and plasma cells, cellularity of the connective tissue in the early stages, desquamation of the epithelium and diffuse and even bilateral distribution of the changes. As cause of the inflammation, they accept either bacterial infection or some unknown irritation.

Those who favor the neoplastic origin stress the importance of the epithelial proliferation with its tendency to metaplasia and finally to malignant degeneration. They consider the changes of the stroma as secondary and unimportant.

12 Sicre. De la maladie cystique de la mamelle. Thèse de Paris 1890

13 Schimmelbusch. Arch. i. klin. Chir. **44** 117 1892

14 Keibel. Berl. klin. Wchnschr. 1904 p. 808

15 Saar. Arch. f. klin. Chir. **84** 223 1907

16 Tietze. Deutsche Ztschr. f. Chir. **56** 512 1900 **75** 117 1904

17 Goens. Contribution à l'étude de la glande mammaire senile et de ses états précancéreux. Thèse de Genève 1919 no. 881

18 Hahn. Virchows Arch. i. path. Anat. **262** 531 1926

19 Askanazy. Schweiz. med. Wchnschr. **55** 1017 1925. Beitr. z. path. Anat. u. z. allg. Path. 1923 vol. 71

In opposition to both theories, a third conception has been brought forth by a large group of other investigators. Already Baird and Lemoine<sup>20</sup> believed that a congenital weakness of the tubular structures accounted for their distention by a slightly increased intraglandular pressure. They called the condition "essential cystic disease of the breast." The developmental theory was more seriously substantiated by the extensive contributions of Krompecher,<sup>21</sup> who emphasized the similarity of certain cells, quite common in the lesions in the breast, to those of the axillary sweat glands. He also claimed that these sweat glands and the breast gland proper are of similar origin in the embryo, while they develop into two different types of glands later. He claimed that groups of glands of the sweat gland type may develop erroneously within the breast tissue and are responsible for the formation of the cysts with those peculiar "pale cells." Krompecher distinguished two stages of the disease: the first with preponderant connective tissue formation and comparatively few small cysts (fibrosis hydrocystica), the second characterized by a large number of more extensive cysts which obscure the development of fibrosis in the stroma (polycystoma hydrocysticum). Krompecher's views are shared in many respects by Aschoff<sup>22</sup> who preferred, however, the name of mastopathia cystica and claimed that irritations, due to physiologic stress but also to pathologic factors, are responsible for this condition.

Cystic disease of the breast has been compared also to the hyperplasia of the prostate in senile persons (Bloodgood<sup>23</sup>), but this comparison does not solve the problem and does not seem to be a lucky one as the cystic disease of the breast occurs at a much earlier period of life. The conception, however, that a process of involution might be responsible for the epithelial changes as well as for the fibrosis seems quite suggestive (Speese and Konjetzny<sup>24</sup>). That involution might be influenced by the lack of hormonal stimulation or by some other endocrine dysfunction is actually conceivable, but could not be substantiated (Pribram<sup>25</sup>, Moskowitz,<sup>26</sup> Dietrich and Kuckens<sup>27</sup>).

20 Baird and Lemoine Arch de med, 1890

21 Krompecher Beitr z path Anat u z allg Path **62** 403, 1916, Virchows Arch f path Anat **250** 495, 1924

22 Aschoff Ergebn d allg Path u path Anat **2** 515, 1897

23 Bloodgood J C Ann Surg **79** 172, 1924, Pathology of Chronic Cystic Mastitis of Female Breast, Arch Surg **3** 445 (Nov.) 1921, Bull Johns Hopkins Hosp, April 1921, Diagnosis of Early Breast Tumors, J A M A **81** 875 (Sept 15) 1923

24 Konjetzny Zentralbl f Chir **50** 1760, 1922, Med Klin **16** 180 1921

25 Pribram Deutsche med Wchnschr **45** 1075, 1919

26 Moskowitz Munchen med Wchnschr **74** 874, 1927, Arch f klin Chir **144** 138, 1927

27 Kuckens Beitr z path Anat u z allg Path **80** 40, 1928

A large number of other authors like Bertels,<sup>28</sup> Mintz,<sup>29</sup> Todvo,<sup>30</sup> Lukowski,<sup>31</sup> Marchand, - Levee and Theile stressed the point that the cystic disease is neither inflammatory nor neoplastic and starts essentially as a hyperplastic condition of the connective tissue with secondary, mostly mechanical interference within the glandular elements. Strangulation of the acini and ducts accounts for the obstruction of the ordinary discharge retention and cyst formation. Subsequent irritation yields inflammatory changes and hyperplastic proliferation of the epithelium.

Other authors particularly Judd,<sup>32</sup> Rodman,<sup>34</sup> Castle, Custone, Porter,<sup>35</sup> Glanman and Hart<sup>36</sup> were more conservative in their statements and refrained from offering any definite conclusion as to the pathogenesis of the disease, yet they all emphasized the tendency of this condition to develop into a malignant process.

#### SUMMARY OF AUTHORS' CASES

From the study of our own cases and in summarizing the observations, we could construct the following picture. Constant features of the disease are fibrosis of the breast gland and cystic dilatation of some of the glandular structures. Other changes are less constant, and their presence or absence seems to be dependent on the state of development in which the diseased breast was removed and examined histologically. It seems to us that the early stages of the condition are characterized by regressive changes of the breast gland which consist of atrophy, on the one hand, and vacuolization and occasional desquamation on the other. Proliferation of the stroma in between the epithelial structures is quite common, but not at all constant (cases 100, 180, 460, 1066, 5266 and 5550).

The second stage in the development of the condition seems to be represented by active proliferation of the epithelial cells. The proliferating cells are larger and conspicuous for a more intensely staining cytoplasm. The staining is decidedly basophilic. This proliferation may set in in glandular units which were not distended previously during the regressive stage, this yields almost solid epithelial nests or

28 Bertels *Deutsche Ztschr f Chir* **124** 9 1913

29 Mintz *Berl klin Wchnschr* 1899, p 1029

30 Todvo *Arch f klin Chir* **104** 440 1914

31 Lukowski *Deutsche Ztschr f Chir* **157** 81 1921

32 Marchand *Munchen med Wchnschr*, 1916, p 396

33 Judd *J Michigan M Soc* **13** 11 1914

34 Rodman *Diseases of the Breast with Special Reference to Cancer* Philadelphia P Blakiston's Son & Company 1921

35 Porter *Surg Gynec Obst* **1** 400, 1905 **31** 584, 1920

36 Hart Deryl *Intracystic Papillomatosis Tumors of the Breast Benign and Malignant* *Arch Surg* **14** 793 (April) 1927

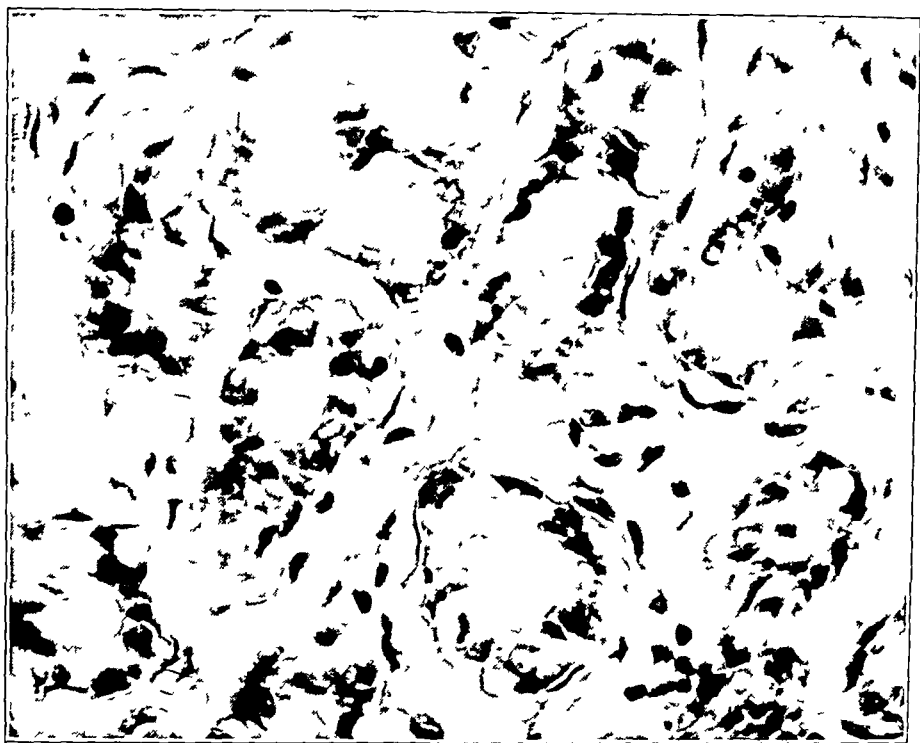


Fig 1—Vacuolization and incipient dilatation of breast gland acini

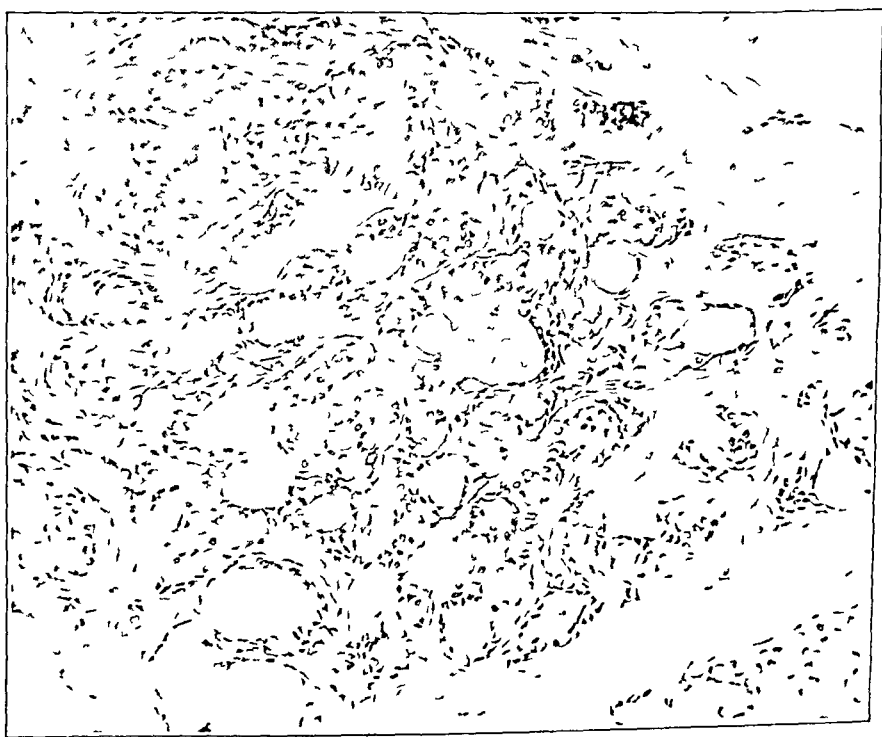


Fig 2—Incipient cystic dilatation of breast gland acini

alveoli. It occurs, however, just as frequently in previously distended tubules, but does not necessarily develop all over their circumference. In such cases one side of the small cyst is lined with flat epithelium, whereas the rest shows multiple layers of larger cells with basophilic staining. The regressive changes, of course, do not subside with the onset of proliferation, and combination of the two is common (cases 354, 460, 468, 500, 606, 671, 700, 1000, 1041, 1066, 1278, 5221 and 12,976).

Further development of the lesion progresses on two main lines: one of which is the formation of larger cysts, whereas the impression of the

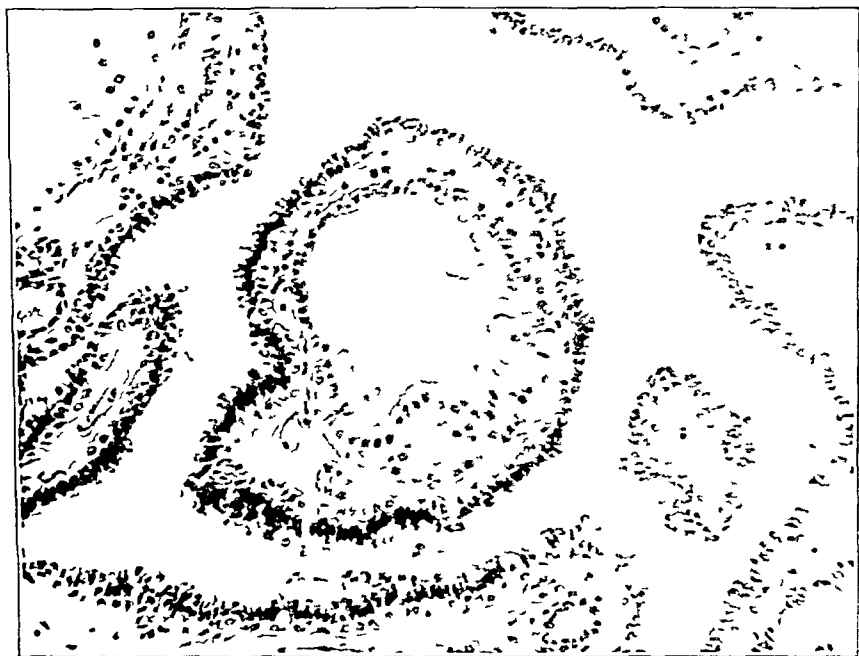


Fig. 3—Development of eosinophil epithelium from ordinary epithelium in papillary cystadenoma.

other is more that of a hyperplastic process of the glandular parenchyma. In the larger cysts and occasionally also in the smaller ones we are impressed by the appearance of large epithelial cells with eosinophil cytoplasm. These cells usually form a single layer in contradistinction to the other cysts in which at least two layers can be distinguished. These cells are usually quite regular, cuboidal or of high columnar shape. Active proliferation of these cells is expressed by real papilli or more frequently by pseudopapilli without any vascular or connective tissue support (cases 53, 460, 500, 1328, 5221 and 5266). These eosinophil or pale cells as they are often referred to are of a fairly homogenous structure, more frequently, however, it is readily visualized



that the eosinophil substance forms intracellularly into small granules or lumps which coalesce later. Part of this hyaline substance is frequently expelled from the cell and found in the lumen as globular hyaline material (cases 215, 606, 1066, 1200, 1278, 5266 and 5550). It is quite common to see cysts of various size with comparatively low lining epithelium which, however, reveals digit-like expansions toward the lumen. These cells already show the onset of intracellular hyalinization, particularly in their expansions, which break off readily. Hyaline globules found in cysts without typical eosinophil epithelium develop from such cells as were first described.

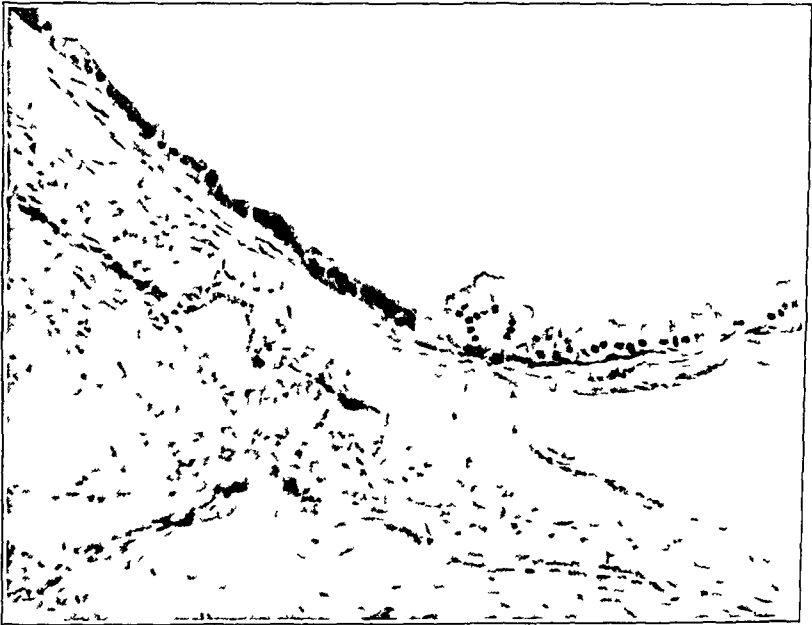


Fig. 4—Large cyst lined partly with eosinophil cells and partly with ordinary low cuboidal epithelium

It is fairly easy to demonstrate a constant line of development from the ordinary lining cell of the cysts over the small cell with digit-like expansion to the fullfledged eosinophil cell. It can be demonstrated also that in one and the same cyst part of the lining cells are of the eosinophil type, whereas the rest consist of ordinary or extremely flattened epithelium. Moreover, one can demonstrate lobules of breast gland tissue in which part of the lobule preserves its ordinary structure, while the rest show some simple cysts and others eosinophil cells. Solid nests consisting of eosinophils are occasionally encountered in such lobules.

Proliferation in the diseased breast gland tissue reaches a remarkable degree in the advanced stages of the condition. The result is the formation of solid alveoli or more often of small cysts with multi-

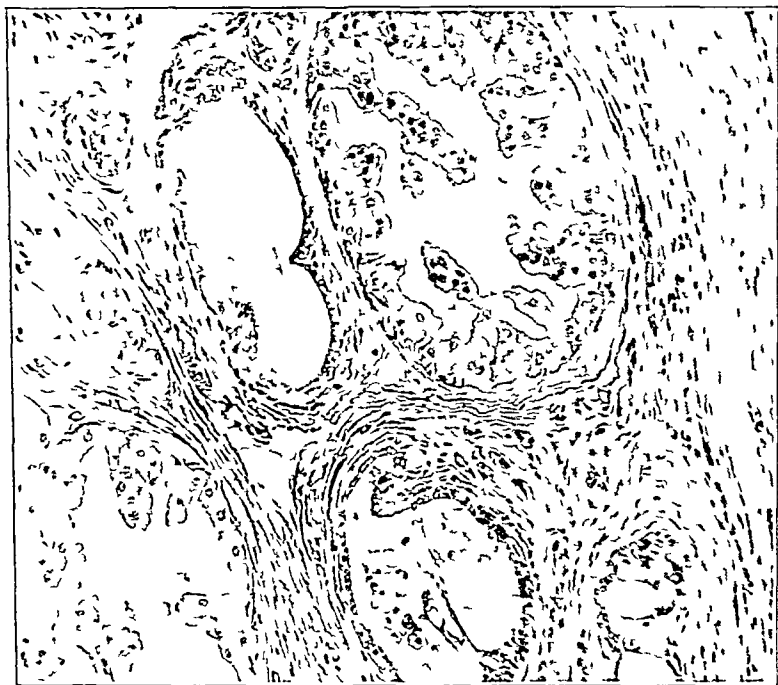


Fig 5—Multiple cysts, some with eosinophil, others with ordinary, epithelium or intermediary cells. Numerous papilli in the eosinophil cysts

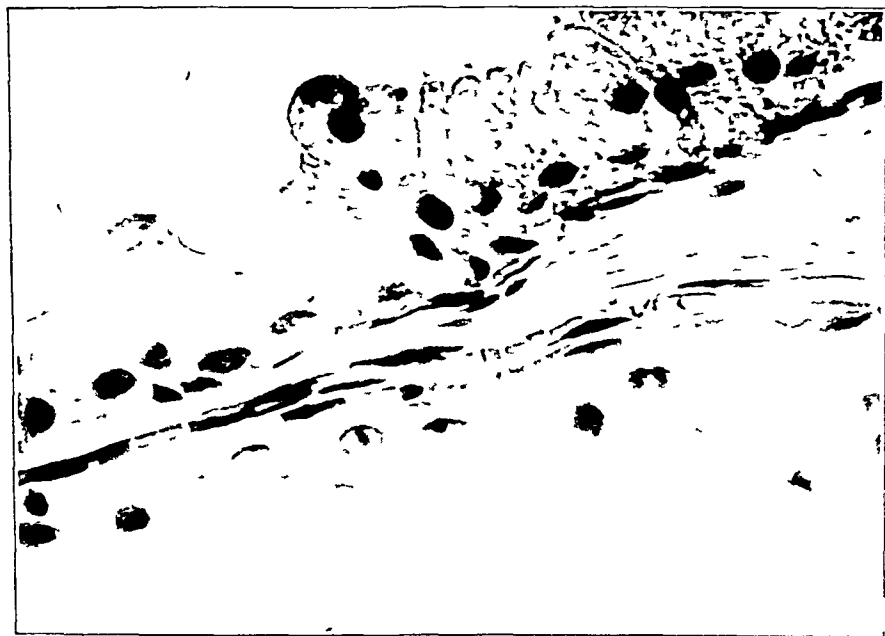


Fig 6—Septum between two adjacent cysts with eosinophil lining. Spindle shaped cells at the base of the epithelium enclose capillary spaces which contain red blood cells

layered epithelium from which peculiar trabeculae spread across the lumen and form a delicate network, until finally the open spaces between these proliferating cells disappear completely (cases 53, 354, 500, 570, 606, 1000, 5221, 5266 and 12,976). Distended cysts with flat, apparently not proliferating, epithelium, papillary cysts, or cysts with trabeculation in their lumen and finally solid alveoli often occur together within the area occupied previously by a single breast gland lobule. Of course, in this stage of proliferation the epithelial growth is not always confined to its original area, and coalescence of several adjacent lobules occasion-

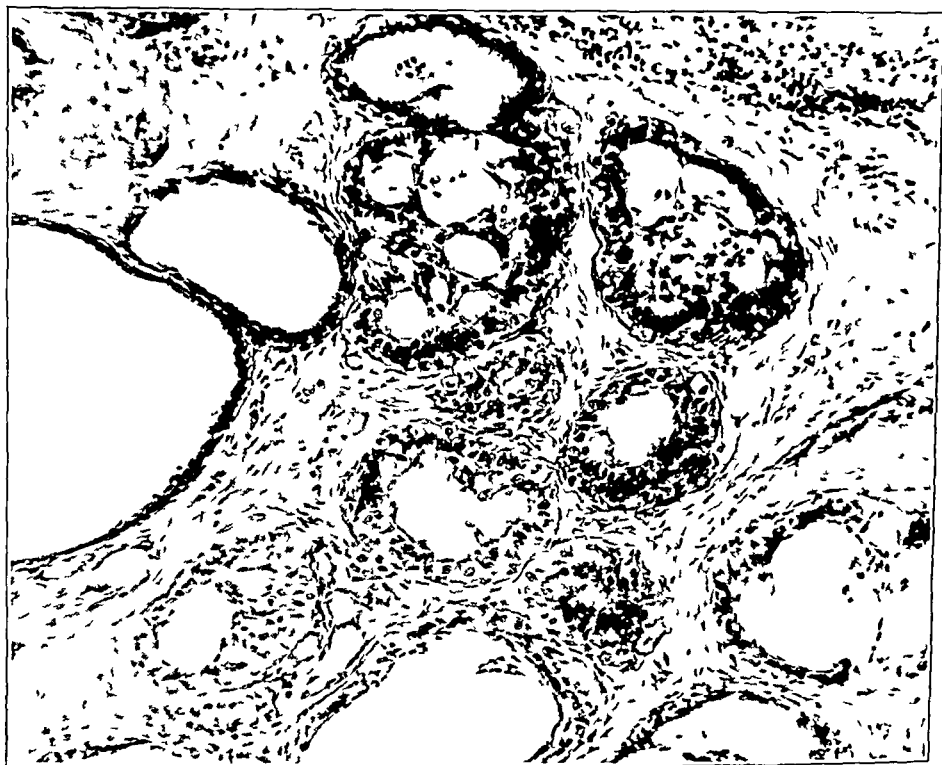


Fig 7—Multiple cysts, hyperplasia of the epithelium with trabeculation

ally produces quite extensive masses with little stroma in between. The amount of stroma is reduced further by coalescence of adjacent cysts. This happens, as it does in many other organs, if the septum between two contiguous cysts is thinned out until it breaks through, whereby the two cysts unite. Remnants of the former septum project into the lumen of the cyst as small spurs.

Extensive hyperplastic vegetation of the cystic breast gland is not always easily distinguished from a neoplastic condition, and a satisfactory classification of the lesion is altogether impossible. It is more a matter of taste, whether one calls the lesion a papillary cystadenoma or cystic hyperplasia. Remnants of fat tissue or atrophic islands of

breast gland embedded in hyaline fibrous tissue in between the papillary cystic structures are suggestive of a hyperplastic condition rather than of an adenomatous neoplastic process

In some of our cases well circumscribed and morphologically well characterized benign neoplasms were present (cases 606, 1000, 1066, 5266, 1750, 1857 and 1932). In two cases the neoplasms were pure adenomas, while in the others, they belonged plainly in the group of ordinary fibro-adenoma. It is impossible to decide whether the origin of these neoplasms had anything to do with the cystic disease of the

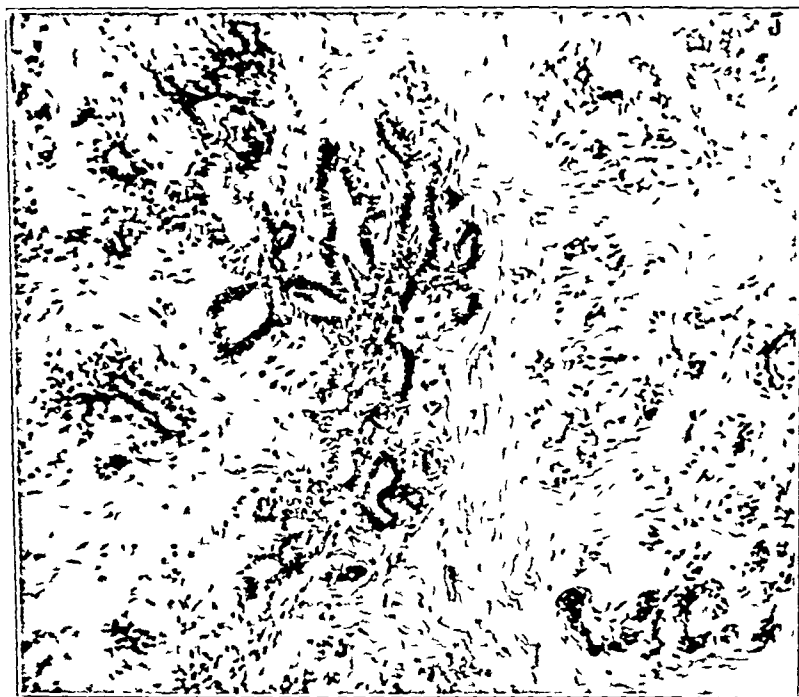


Fig 8—Hyperplastic breast gland with proliferating epithelium

breast gland, the presence of the tumors may have been merely incidental

Mammary carcinoma was more frequent in our material (cases 53, 354, 500, 570, 741, 1908, 4000, 5273, 5550, 7010, 11,010 and 12,976, and the character of the changes observed seems to point to a certain relationship between the hyperplastic processes in the breast gland and the later development of carcinoma. In some of the cases the carcinoma was fairly cellular and alveolar in structure, yet the formation of cysts within the carcinomatous alveoli was quite conspicuous. The carcinomatous nature of these tumors was unquestionable, in view of their infiltrative growth and the morphologic appearance of the cells. Still

there were areas in which the anaplasia of the tumor cells was not so distinct and in which the resemblance to the hyperplastic forms of the cystic breast gland appeared particularly striking. In the midst of the cancer tissue were cysts lined with flat epithelium or with flat epithelium on one side and solid groups of tumor cells on the other. Transitions between the two cell types were common. They and the general structure of the tissue excluded the possibility that we were dealing with an invasion of the preexisting cysts by cancer cells. Other areas of the same breast showed changes which were certainly not neoplastic

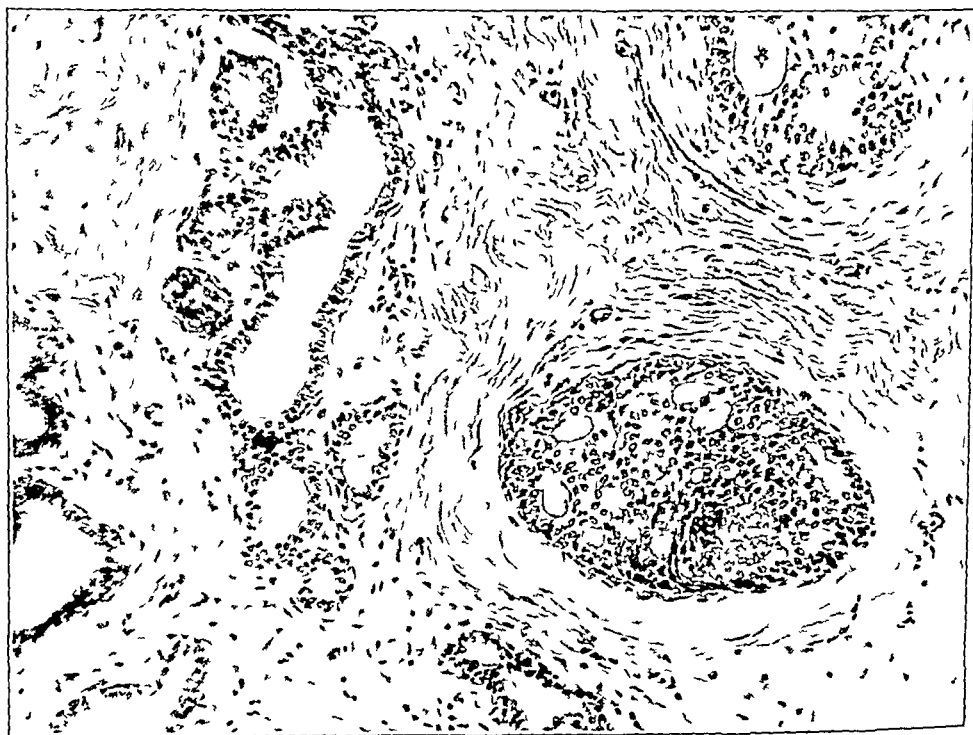


Fig 9—Solid epithelial structure with several small lumina

and were classified with those commonly observed in cystic breasts. Hyperplasia in this definitely not neoplastic condition varies greatly as to its intensity and forms a continuous chain until it assumes the character of an infiltrating malignant growth. There seems to be conclusive evidence that the carcinoma develops from multiple centers within the breast, with gradual transition between the hyperplastic and the carcinomatous foci. We are left in doubt occasionally whether the process should be considered already as carcinomatous or still as hyperplastic. We classify these changes, therefore, as precancerous. It is noteworthy that carcinoma developing in a hyperplastic cystic breast is prone to imitate the structure of its matrix, and the cells of the car-

cinoma differentiate occasionally well enough to simulate those of the hyperplastic breast gland

The importance of the relationship between carcinoma and the cystic changes was emphasized in our material in several cases (462, 1121, 1406 and 5221) in which we could not demonstrate real infiltrative growths, yet the morphologic appearance of the hyperplastic epithelium was already suggestive of carcinomatous tissue. We considered these as precancerous changes. As a matter of fact they were identical with changes that are readily observed in the vicinity of frank carcinomatous

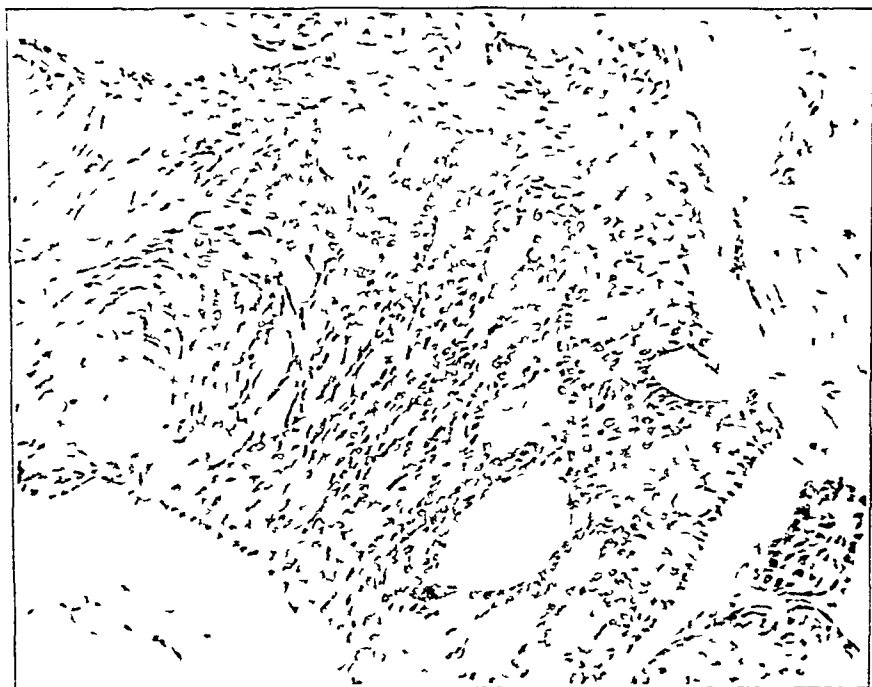


Fig 10—Medullary carcinoma of the breast resembling epithelial proliferation in cystic cirrhosis

foci. Whether these precancerous changes were about to develop really invasive tendencies remains to be proved, although it seems highly probable.

One of the most contested questions is the importance and frequency of fibrosis in a breast with cystic changes. Extensive fibrosis was present in thirty-two of our own cases, while in four fibrosis was but part of a chronic productive and suppurative process. Fibrosis was of less extent and prevalence in the other cases. These figures show that the coincidence of real inflammatory changes with cystic disease of the breast is rare, which makes their rôle in the pathogenesis of the disease at least questionable. Fibrosis, on the other hand, without evi-

dence of inflammatory changes is so common and is present in so many cases to such an extent that a pathogenic connection between fibrosis and cystic disease seems to be logical

Fibrosis of noninflammatory origin could be the result of senile atrophy. But the age of our patients does not justify the assumption of senile involution. As a matter of fact, fibrosis of the breast in comparatively young women has been observed by us as well as by others. This would rule out senile involution and would leave only one explanation, that is, development of fibrosis on the basis of regressive changes of the breast gland with substitution of the decaying parenchyma by connective tissue. This conception is borne out by morphologic evidence as well as by physiologic considerations. Regressive changes of the breast gland were easily demonstrable in many of our cases. They include vacuolization due to intracellular hydrops or deposit of fat, and formation of hyalin in the cytoplasm with discharge of hyaline droplets into the lumen. They may result in the breaking up of the impaired cells. Dilatation of the glandular structures on account of retention brings pressure to bear on the lining cells which assume subsequently a more flat shape, so much so, that they resemble endothelial cells.

Breast glands presenting such regressive changes with or without cystic dilatation are usually surrounded by loose connective tissue which invades the lobules and tries to separate the individual glands. The glands are less and less numerous in the advanced stage until most of the lobule is substituted by connective tissue. Yet the outlines of the lobule are still maintained and marked by a ring of dense hyaline connective tissue fibrils. Sometimes part of the lobule is fibrosed and contains but a few discrete glands, while other parts of the same lobule are practically unaltered or show only incipient degenerative changes.

Regressive changes of the breast gland are physiologic, particularly after pregnancy, as involution succeeds the massive hyperplasia of gestation. Similar changes, although much less conspicuous, are observed during the course of menstruation (Loeb,<sup>37</sup> Rosenberg<sup>38</sup>). It is true that the authors are not in accord about the extent and the importance of the menstrual changes of the breast gland. Yet clinical evidence already shows that the breast gland participates in the physiologic changes of the menstrual cycle. On the other hand, it seems that the extent of these changes varies individually.

The morphologic changes of the breast gland which have been described as occurring during menstruation are quite comparable to those observed in fibrosis of the breast gland. The similarity is enhanced by the fact that hyperplastic processes alternate with the regressive

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37 Loeb and Hesselberg. *J Exper Med* 25:285, 1917.

38 Rosenberg. *Frankfurt Ztschr f Path* 37:466, 1922.

changes. The only but apparently essential difference is the formation of interglandular connective tissue with subsequent hyalinization. The onset of regeneration with epithelial hyperplasia is obviously interfered with by the presence of massive connective tissue formed between the glands. Cystic dilatation is most probably also closely connected with the interstitial process as mechanical dilatation (retraction of shrinking hyaline fibrils) plays a role in addition to that played by retention of glandular discharge.

It is illuminating to compare the observations just described, characteristic of mammary fibrosis with similar changes in other glandular

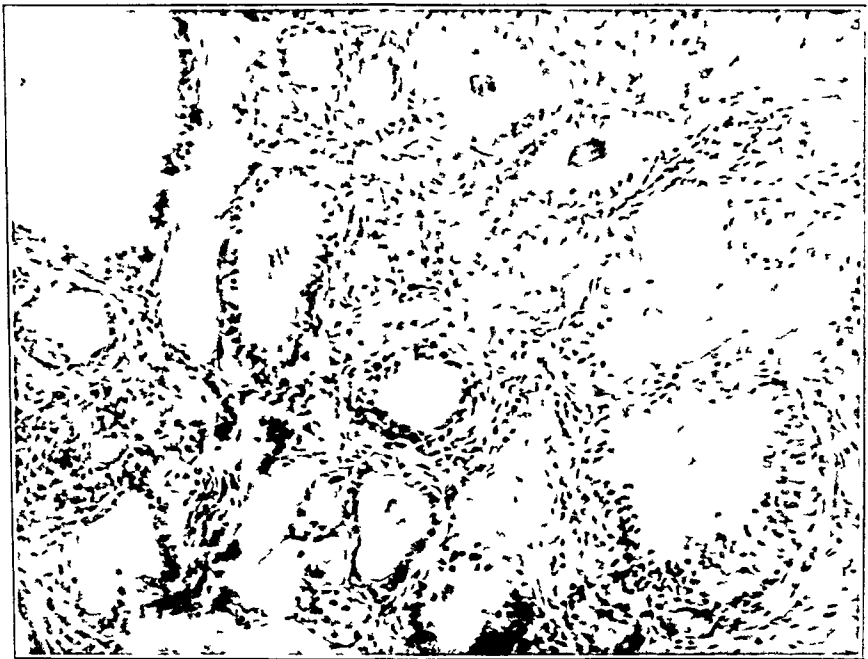


Fig. 11—Adenocarcinoma of the breast simulating the glandular structures of cystic cirrhosis

organs such as the liver. Liver cells degenerate and disappear frequently under physiologic conditions. They are easily replaced by proliferation of adjacent cells, or by new formation of liver cells at a distance with readjustment of the architecture. If the disappearing liver cells are not replaced by their own kind, either owing to lack of regenerative power or to the excessive volume of the defect, connective tissue takes up the space of the lost parenchyma. Hyperplasia of the periportal connective tissue is concomitant. Interstitial fibrosis is often followed by more or less substantial hyperplasia of the persisting liver parenchyma which may terminate in the formation of nodules practically identical with liver cell adenoma.



These changes, if fully developed, constitute the histologic picture of cirrhosis of the liver and justify the following definition of the condition regressive changes of liver cells, substitution of the lost parenchyma by scar tissue and secondary hyperplasia of the persisting epithelial elements (Kietz). The analogy between the changes constituting cirrhosis of the liver and those characteristic of the cystic disease of the breast is striking. This analogy goes even farther and applies also to the relationship of both conditions to neoplastic processes. The relationship of nodular hyperplasia and adenoma occurring in cirrhosis of the liver to liver cell carcinoma has been dealt with extensively before by one of us<sup>30</sup>. It is generally accepted now that liver cell carcinoma develops in the overwhelming majority of cases from previous hyperplasia which had developed in the course of cirrhosis. When the histogenesis of cirrhosis of the liver is compared with nodular hyperplasia and its occasional transformation into liver cell carcinoma, on the one hand, with fibrosis of the breast, cystic hyperplasia and finally the development of adenocarcinoma on the other, the almost parallel behavior of the two different tissues is striking. It seems, therefore, that the term "cystic cirrhosis of the breast" appropriately describes the real nature of the process and emphasizes that its histogenesis is analogous to similar conditions in other organs. The only difference between cirrhosis in the liver and that in the breast is the cystic character of the lesion in the latter. This, however, is understood without difficulty by comparing the two different matrices, the acinous glands of the breast and the solid trabeculae of the liver parenchyma.

What we propose to call cystic cirrhosis of the breast has been given so many names already by other authors that a new name seems superfluous. Yet most of these names are misleading, being based on erroneous assumptions or misinterpretations, others do not imply the essential characteristics of the condition. Polycystoma, for instance, suggests a neoplastic condition, hydrocystoma and its various modifications, as suggested by Krompecher, are based on the assumption that the lesion develops from aberrant sweat glands, cystic disease of the breast is noncommittal and therefore is a name of little value.

Among the varied features of cystic cirrhosis, the appearance of eosinophil cells has been most puzzling. These cells are also spoken of as "pale cells," probably because when van Gieson's method is used, they stain a faint yellow. The fully developed pale cell resembles the sweat glands of the epithelium. Yet these cells are large and assume peculiar staining properties on account of accumulation of some probably albuminous matter in their cytoplasm which we interpreted as the

expression of a metabolic disturbance. The early stage of these changes is readily demonstrable in some of the glands of otherwise unchanged breast tissue. The same is observed occasionally in fibro-adenoma of the breast. We could show also transitions between eosinophil and ordinary epithelium in cysts that were lined partly with fully developed eosinophil cells and partly with ordinary or flat epithelium. Krompecher tried to substantiate the sweat gland nature of the eosinophil epithelium by calling attention to the presence of a layer of spindle-shaped cells which surrounds the eosinophil cysts. He interpreted these cells as smooth muscle elements. He identified them with the muscle cells which are an intrinsic part of the sweat gland structure. However, their interpretation as muscle cells is not convincing. Moreover, we were able to show that some of these cells line capillary spaces which run parallel to the wall of the cyst. Some of these capillaries contain red blood cells, while others are empty and seem to be only lymph spaces. Thus it is fair to classify these cells with endothelium and to reject Krompecher's developmental theory which is based on the mere morphologic resemblance of the pale cells and spindle cells to the constituents of sweat glands. The striking resemblance between these pathologic elements of the diseased breast and those of the sweat glands is elucidated by referring once more to the analogy between cystic cirrhosis of the breast and cirrhosis of the liver. Liver cells, after having undergone regressive changes are prone to assume the appearance of bile duct epithelium. Whole trabeculae of liver cells are transformed occasionally into structures that simulate small bile ducts. This process has been interpreted as a reversion of the liver cells by loss of differentiation to a more primitive cell type. Such pseudobile ducts are prone again to develop progressive changes, and they participate in the formation of both new liver tissue and tubular adenomatous structures.

The occurrence of similar metaplastic changes in the breast gland is well conceivable. The breast gland cell may also lose its differentiation and revert thereby to a more primitive type which is the common matrix of both breast and sweat gland cells. If differentiation sets in again, the newly produced tissue may easily assume the sweat gland type. Similar indirect metaplasia is known to occur in other glandular organs or on mucous membranes. The assumption of indirect metaplasia seems to us a much more likely explanation of the sweat gland-like structures in the breast than the hypothetical misplacement or malformation of sweat glands. Yet we also believe that it is not necessary to fall back on the assumption of indirect metaplasia, as metabolic disturbances of the breast gland cells account for changes that are morphologically identical.

## CONCLUSIONS

1 Forty-seven cases in which breast glands were removed surgically were studied

2 The development of cysts in the breast was presented as a primary degenerative lesion associated with perilobular and intralobular fibrosis and completed by hyperplastic changes of the epithelium

3 "Cystic cirrhosis of the breast" is suggested as a more adequate terminology

4 The development of eosinophil epithelium is interpreted as a metabolic disturbance of the breast gland cells, which thereby simulate the appearance of sweat gland epithelium. The process is suggestive of indirect metaplasia and does not warrant the assumption of developmental errors

5 Hyperplastic changes of the epithelium frequently assume the character of precancerous lesions

6 The frequent coincidence of cystic cirrhosis, precancerous changes and carcinoma emphasizes the importance of cystic cirrhosis in the pathogenesis of carcinoma of the breast

7 The histogenesis of cystic cirrhosis of the breast is analogous to cirrhosis of the liver. The analogy is enhanced by the frequency with which adenomatous and carcinomatous neoplasia develops from the originally hyperplastic condition

# CARCINOMA OF THE LARGE BOWEL NOT INCLUDING THE RECTUM AND THE RECTOSIGMOID

CHOICE OF OPERATIVE PROCEDURE \*

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Operation for radical cure of carcinoma of the large bowel is a hazardous procedure. The early mortality was high but has been lowered slowly by the development of the stage operations as well as by proper preoperative preparation and postoperative care. Further decrease in operative mortality and increase in postoperative longevity can be accomplished by standardization of operative procedures. This can be accomplished only when the factors relative to death following operation and to the recurrence of carcinoma are generally known. The factors vary with the locations of the lesions in the large bowel.

## GENERAL CHARACTERISTICS

*Incidence*—It is interesting to note the incidence of carcinoma of the large bowel compared to that of other parts of the body. By statistics this is shown to be increasing. In a series of nearly 70,000 autopsies, Notlmagel, Azerman, Muehler and Madvl found 5,796 deaths from carcinoma. One fourth of the cancers causing death were located in the intestinal canal. 35 were in the cecum, 83 in the sigmoid, 131 in other parts of the colon, and 262 in the rectum. The colon is the site of more cancers than any other portion of the alimentary tract, with the exception of the stomach.

The frequency of occurrence of carcinoma in the several portions of the colon is shown by Judd in a report of 333 cases. In a report of 333 cancers of the colon, he gives the location as follows: cecum and ascending colon, 159 (47.4 per cent), hepatic flexure, 29 (8.7 per cent), descending colon, 75 (22.5 per cent). He also reported 292 cases occurring in the sigmoid flexure. This series closely corresponds to the series of Erdmann and Lockhart-Mummery.

The statistics of Crumpton and Canderceer, Clood, Debocis and the Mayo Clinic show that males are afflicted in a proportion of approximately two to one.

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\* From the Department of Surgery, Woodland Clinic.

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*Occurrence in Decades of Life*—Carcinoma of the large bowel may occur at any age, and, although it is usually found in the fifth and sixth decades, it is not unusual to find it in the second decade, and numerous cases are reported in which the patients were between 20 and 30 years of age. Cases have been reported in which the patients were 3, 5, 14 and 15 years of age.

*Pathology*—The anatomic types of carcinoma of the colon are (1) the soft medullary adenocarcinoma, (2) the scirrhous or fibrosarcoma and (3) the colloid. The different pathologic types are responsible for the wide variations in the symptoms as well as in the roentgenologic observations. Cancers of the right half of the colon, as a rule, are large and irregular and are covered with stubby protuberances. They frequently ulcerate and often produce large masses. In a study of the mortality and recurrence in 203 patients with colloid carcinoma of the gastro-intestinal tract, Parnham found a greater longevity, but a greater eventual mortality. Obstruction is not common, except by reason of adhesions of secondary intussusception. In the colloid type the epithelium frequently forms glands, the lumina of which may be greatly distended by secretion. The glandular type is the least rapidly fatal, owing to the tendency of the secretion to interfere with the nutrition of the cancer cells.

The scirrhous type is chiefly composed of adenocarcinomatous islands surrounded by dense connective tissue. The tumor mass is usually small and annular. Obstruction is, as a rule, an early symptom. The usual site of the tumor is in the left quadrant.

Cancers vary greatly in their degree of malignancy, as was pointed out by Broders in his index of the grading of malignancy. The degree of malignancy is based on the differentiation of the neoplastic cell. The more nearly the cell approaches the embryonic, or undifferentiated, type, the more malignant the tumor. The converse is true, namely, that the more nearly normal the tumor cell is, the lower is the degree of malignancy.

The extension of malignancy from the primary growth is by way of the lymphatics or the blood stream, by cellular implants on the mucous membrane or the serosa of the wall of the bowel and by direct extension.

Jamison and Dobson divided the lymphatics into four groups: (1) the epicolic group commencing with the surface of the bowel (fig 1), (2) the paracolic group in the mesocolon, close to the bowel (fig 1), (3) the intermediate group along the colic arteries (fig 1), and (4) the main glands at the origin of the main artery (fig 2).

The lymphatics as a rule, follow well defined lines, usually accompanying the blood vessels of the part (fig 1) The lymphatic supply of the cecum and ascending colon is extensive when compared to the rest of the colon. It seems to act as a defensive mechanism since metastases occur more slowly there than in any other portion of the large

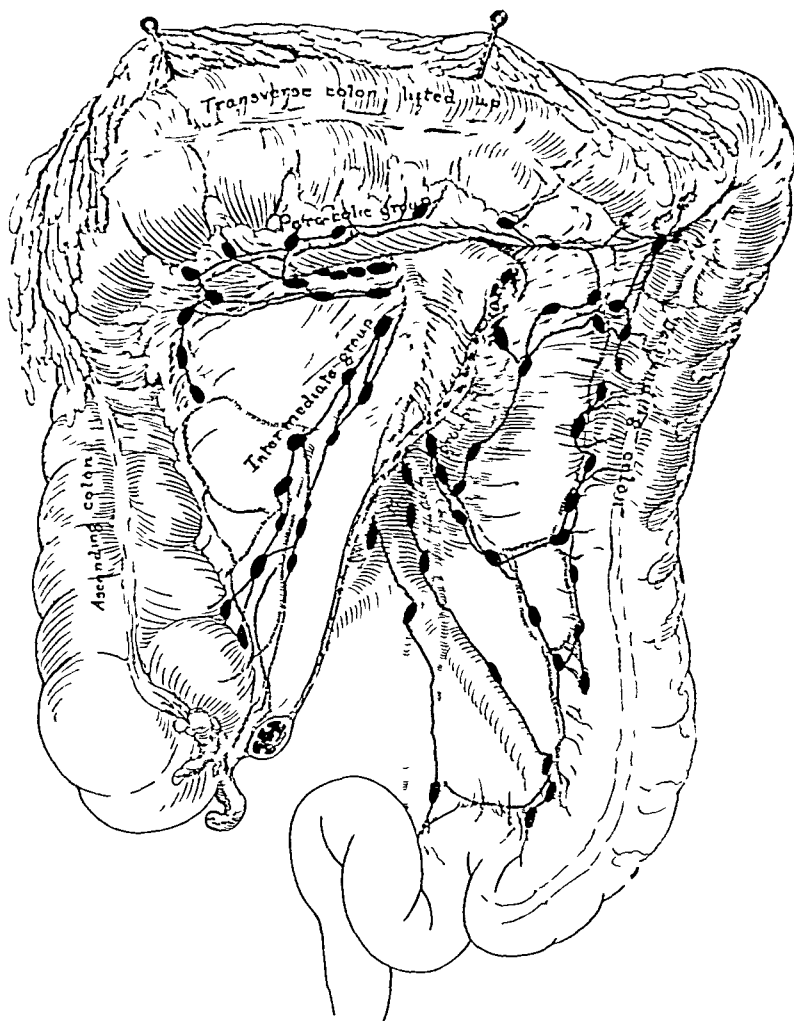


Fig 1—Lymphatics of large bowel

bowel. The lymphatic supply of the descending portion of the large bowel is the least of any of the segments.

In a study of 100 specimens of colonic cancer, Haves observed metastases in the order of frequency to occur in the sigmoid, descending colon, transverse colon, hepatic flexure, splenic flexure and ascending colon. Early metastasis to the liver without appreciable local glandular

involvement is usually an accidental involvement by way of the larger venous tracts. Cancer cells that break off are carried directly to the liver at an early stage of the disease.

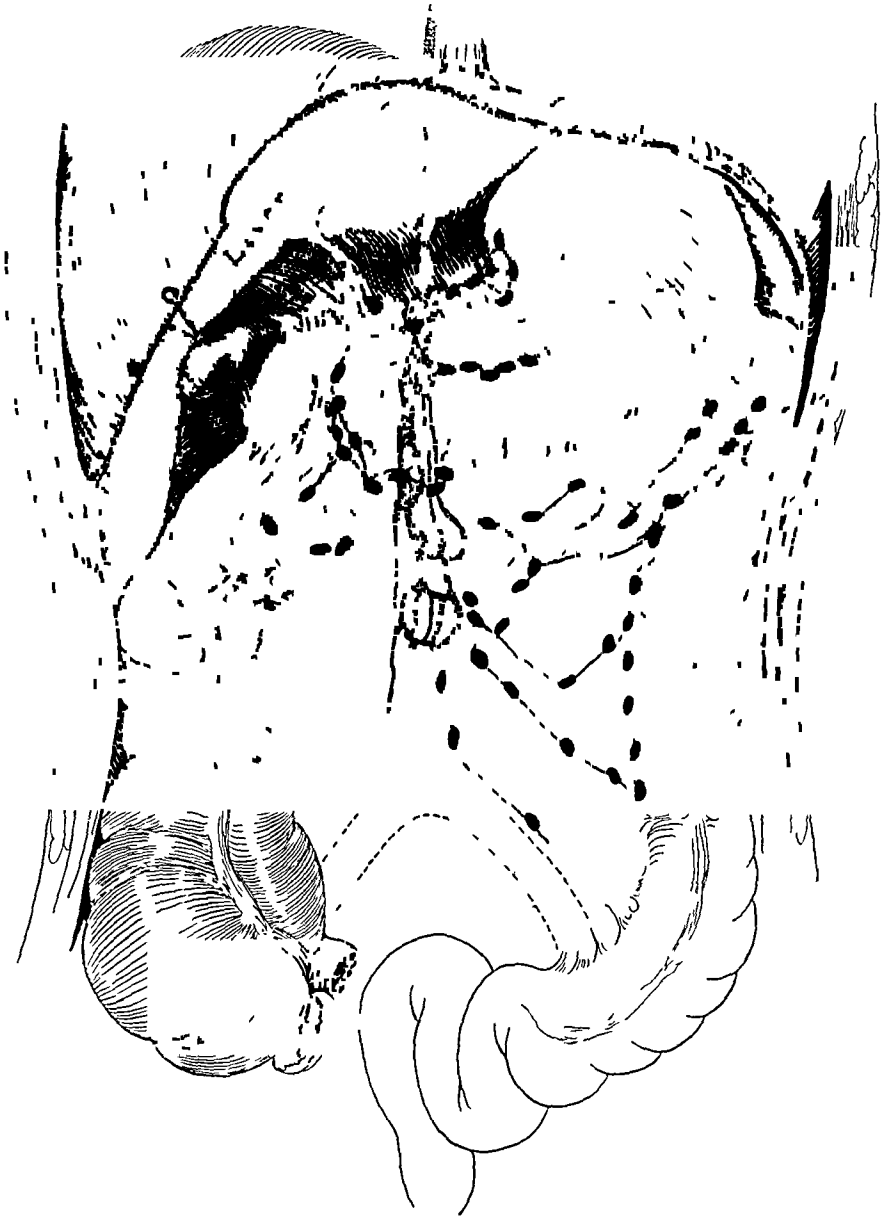


Fig. 2—Relationship of lymphatic drainage to cisterna chyli and portal circulation

Metastatic implants on the inside of the bowel usually occur by back pressure and peristalsis. Masses of carcinoma cells which have been broken off the original tumor are often implanted several inches away from the primary growth.

Carcinoma cells breaking off from the serous surface may likewise find lodgment at distant parts of the abdomen by gravity, often low in the pelvis.

*Location of Lesion*—Roentgenologists are agreed that the barium sulphate enema is the most efficacious method for exact localization of

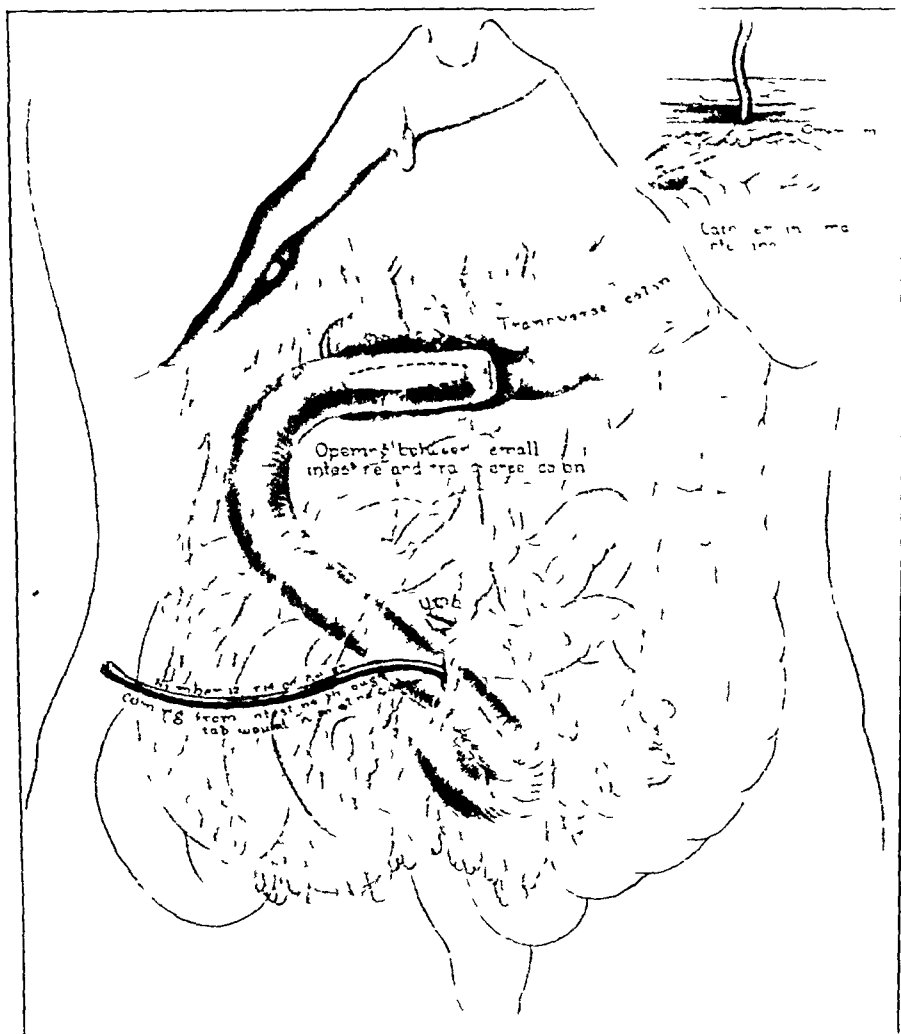


Fig 3—Plan of resection involving right half of colon

the carcinomatous lesion. It is inadvisable to give barium by mouth if obstructive symptoms have been at all marked, owing to the impaction of this material above the lesion. Unfortunately, obstruction is the first symptom noted. The patient so afflicted may become markedly debilitated before surgical measures are instituted. In this instance



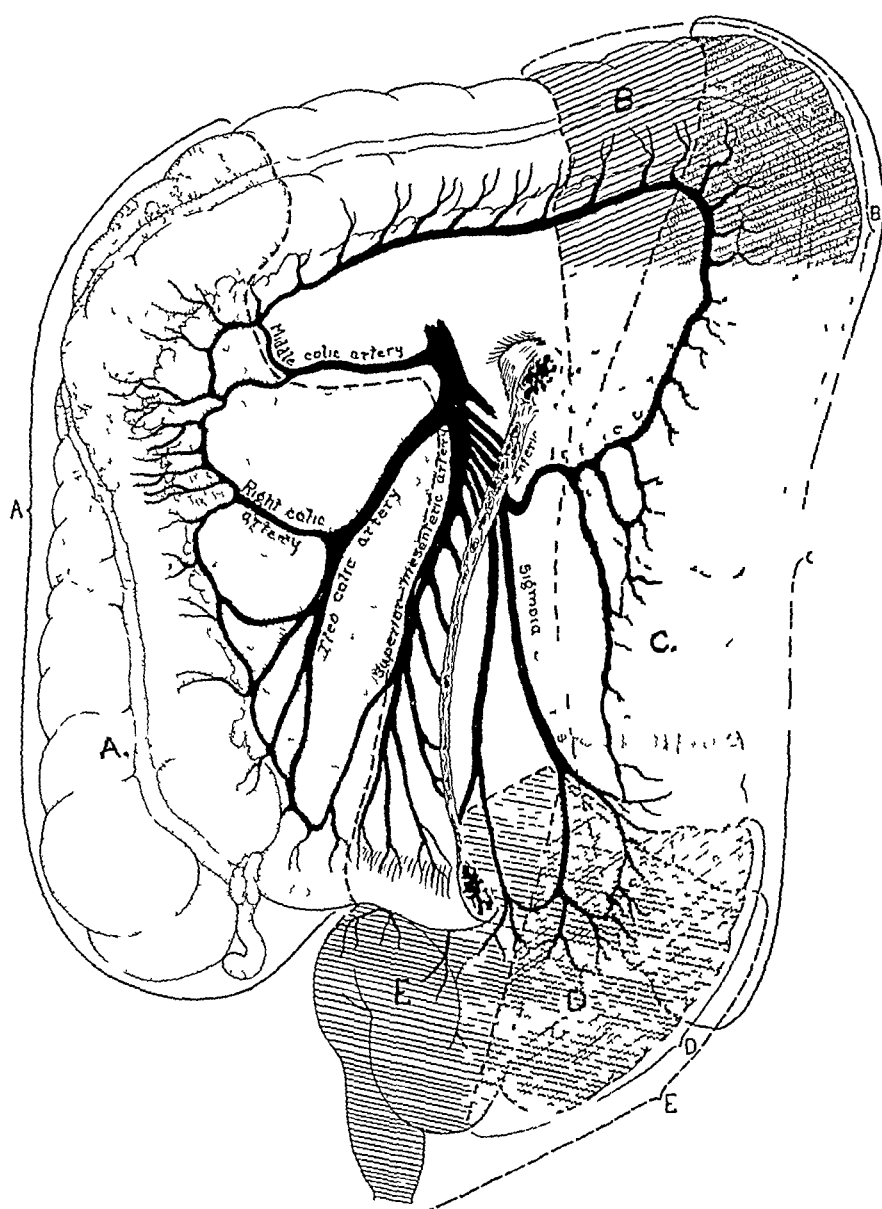


Fig 4—Defined areas of resection according to blood supply of large bowel. *A* indicates area of bowel to be resected in carcinoma of cecum, ascending colon and hepatic flexor, the area between *A-B* to be resected for carcinoma of the transverse colon to save, if possible, the middle colic artery. *B*, area to be resected for carcinoma of the splenic flexor of colon. *C*, area to be resected in ascending colon if extensive glandular metastasis exists. *D*, area which may be resected if small early carcinoma of the sigmoid exists. and *E*, usual area for abdominal perineal resection of the sigmoid and rectum.

extensive examination should not be done and cecostomy or ileostomy under local or regional anesthesia without exploration is the procedure of choice.

#### OPERATION

*Preoperative Preparation*—The initial efforts should be directed toward the correction of obstruction if it exists and toward the restoration of body fluids.

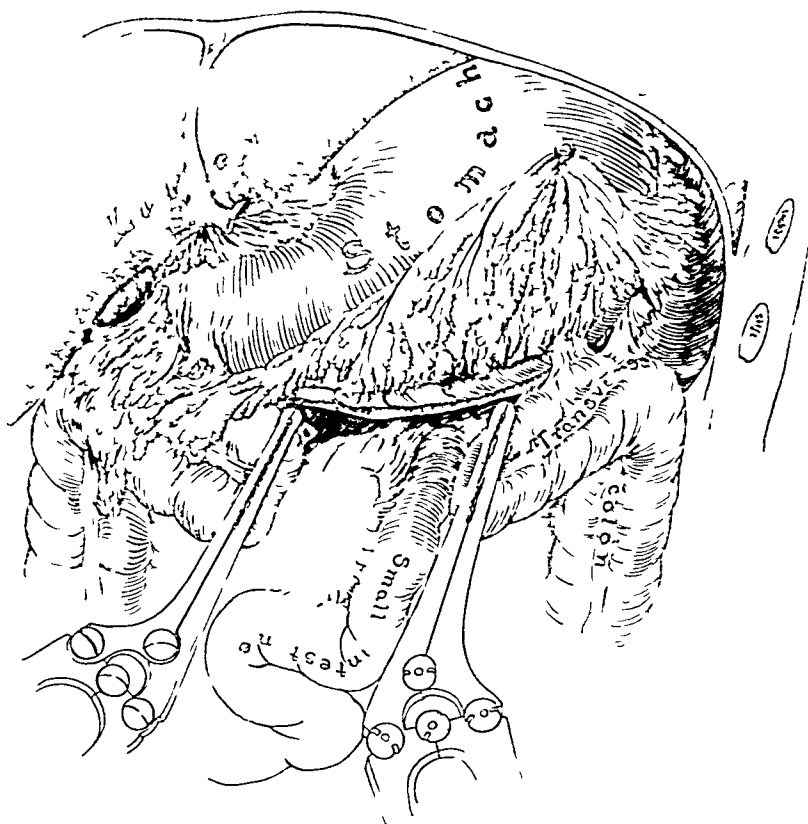


Fig 5—Resection of middle portion of transverse colon showing anatomic relationship and ends ready for choice of anastomosis.

Marked anemia exists in many instances, associated with lesions in the right quadrant. Repeated transfusions may be necessary. Chronic myocarditis, chronic nephritis and hypertension are not unusual complications. Prolonged obstruction with resulting toxemia may greatly damage an already defective cardiorenal mechanism. Examination of the blood urea and nonprotein nitrogen and phenolphthalein tests should be made to ascertain how the kidney is functioning. Before an operation of such magnitude as resection of the bowel is considered, electrocardiographic studies of the heart should be made if myocardial damage

exists Operability can be determined only by careful abdominal exploration after the lesion has been localized by barium enemas However, exploration of the abdomen should not be done without careful preparation when any appreciable degree of obstruction exists, nor is prolonged exploration well tolerated when debility is marked

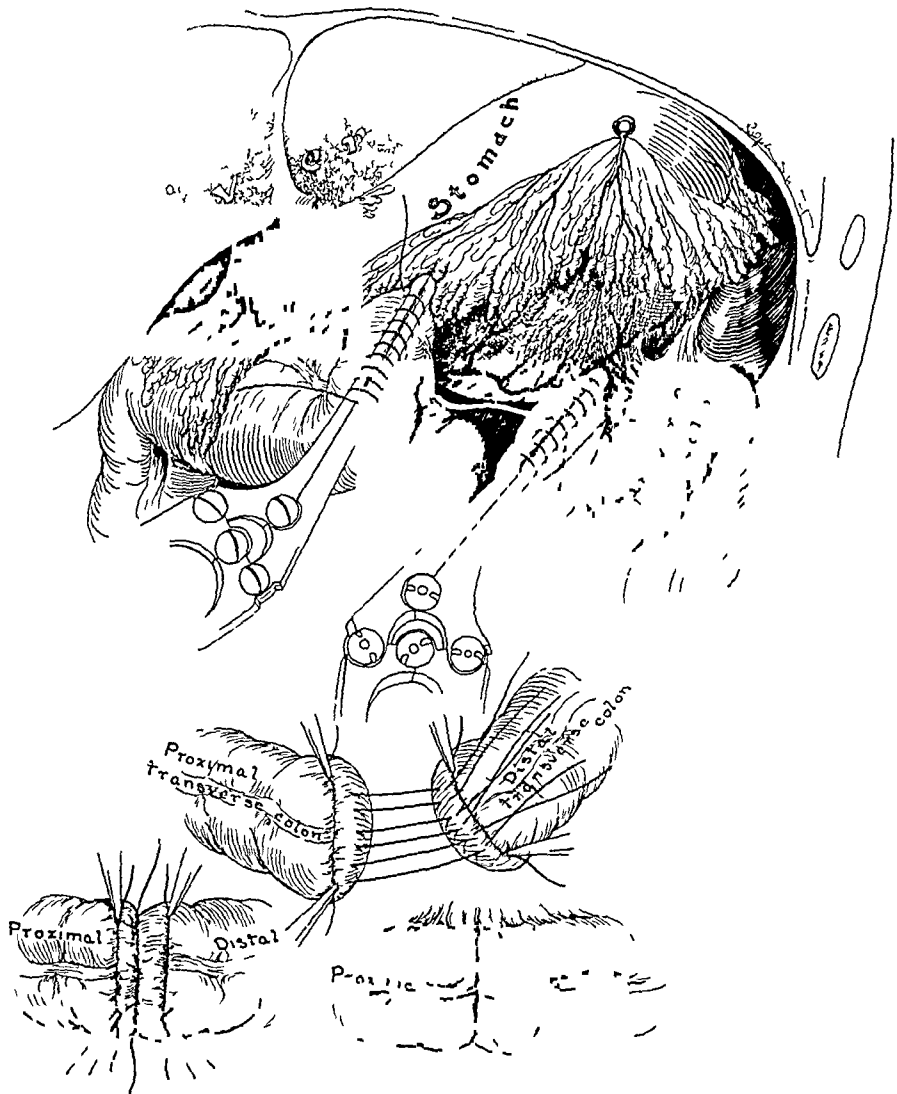


Fig 6—Parker-Kerr closed technic of resection of transverse colon

Surgeons are universally agreed that operation by well defined stages should be instituted in the presence of obstruction Cecostomy or ileostomy through a small incision, under local anesthesia, is then the procedure of choice in preparation

Postoperative herniations and extensive wound infections are common complications when an ileostomy or cecostomy is done through the incision for exploration

Lesions that are immobile before drainage of the bowel may become mobile in from two to three weeks owing to the subsidence of inflammatory reactions.

*Choice of Procedure*—In planning an operation for radical cure of carcinoma of the bowel it is necessary to have clearly in mind both the immediate and the ultimate causes of death, as previously pointed out. Before the advent of the two-stage operation for prostatectomy the postoperative mortality was very high. The mortality was primarily caused by urinary obstruction and was secondary to infection. So it is with obstructive lesions in the large bowel, with infection playing an even more important role. Infection at the time of operation is usually easily overcome by the patient if average aseptic technic has been

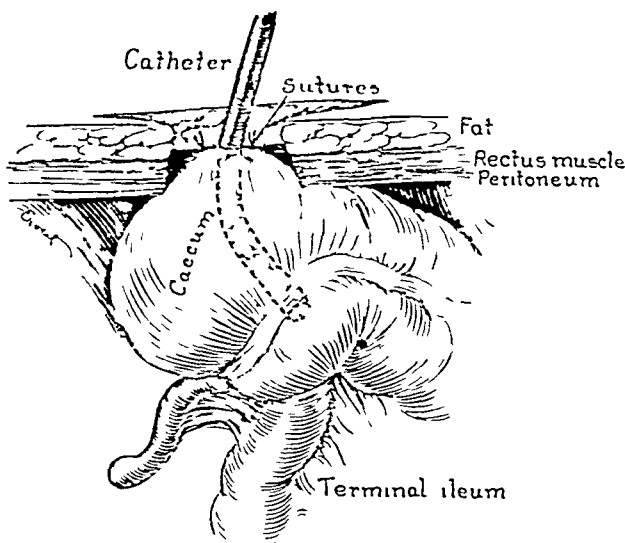


Fig 7—Technic of cecostomy through as small an opening as possible

observed. The large percentage of immediate death occurs from one of the following causes: (1) the resulting paresis and obstruction of the bowel at the operative site from gas pressure, (2) improper selection of the area of resection and the resulting gangrene of the bowel from lack of blood supply, with resulting peritonitis, (3) infection and abscess formation in the wall of the bowel at the site of the suture line, if extensive fat deposits exist, and (4) institution of radical operative procedure before sufficient preoperative preparation has been accomplished.

The less common causes of immediate death are (1) pneumonia if ether anesthesia or prolonged gas anesthesia is used, (2) postoperative shock from prolonged operative procedure or hemorrhage, (3) pulmonary embolus and (4) thrombosis of vessels when tumors have been dealt with by the Mikulicz and Paul methods.

The ultimate cause of death is from recurrence of the carcinoma. Recurrence can be minimized if radical resection is instituted in the

cases considered operable. Consideration of lymphatic and blood supply of the large bowel cannot be overemphasized in considering the segment of bowel to be resected.

Carcinoma of the cecum, ascending colon and hepatic flexure usually is not markedly obstructive. If obstruction does not exist, a primary

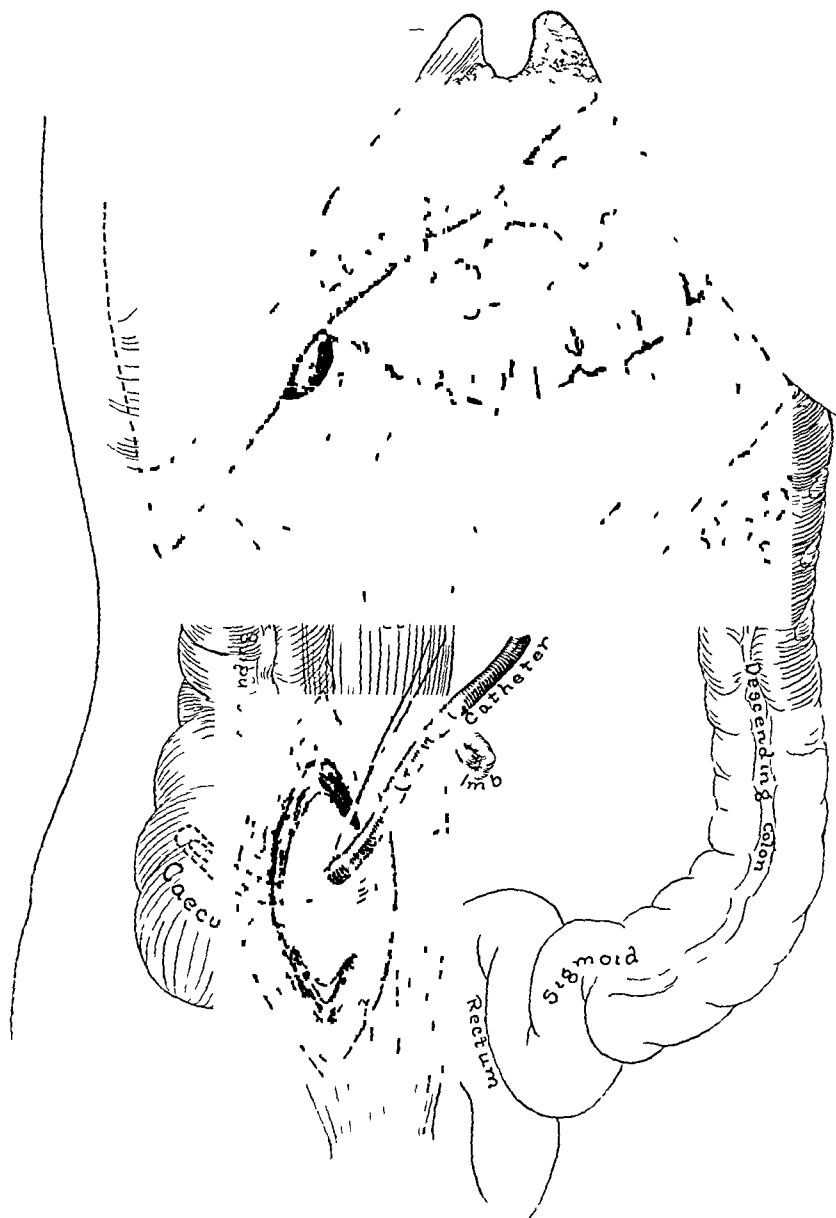


Fig 8—Position of cecostomy in relationship to tumor mass

resection can usually be done (fig 3). This operative procedure is unquestionably the safest when the factors of blood supply (fig 4) and lymphatic supply (figs 1 and 2) are considered. The extent of the resection is shown as *A* in figure 4. Supplementary ileostomy is

advisable at a point removed from the incision if obstruction exists to any considerable degree at the time of primary resection.

Carcinoma arising in the transverse colon can be dealt with by a primary resection (figs 5 and 6). Cecostomy (fig 7) or ileostomy is advisable if the patient is old or the obstruction is appreciable. Partial

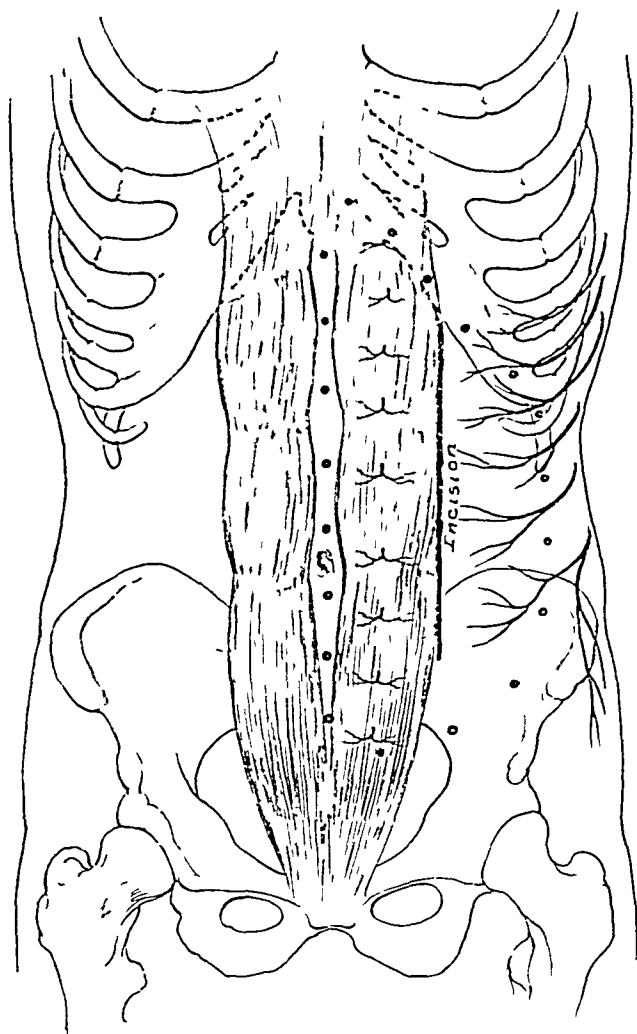


Fig 9—Areas of infiltration of the abdominal wall for exploration and resection of tumor of colon under anesthesia

obstruction that is not greatly improved by medical management should have a preliminary cecostomy done.

Due to the extensive mobilization of the splenic flexure, lateral anastomosis, supplemented by a preliminary cecostomy, is, as a rule, the operation of choice.

Carcinoma of the splenic flexure usually produces obstruction, which is the outstanding symptom. The blood supply is poor (fig 4 B).

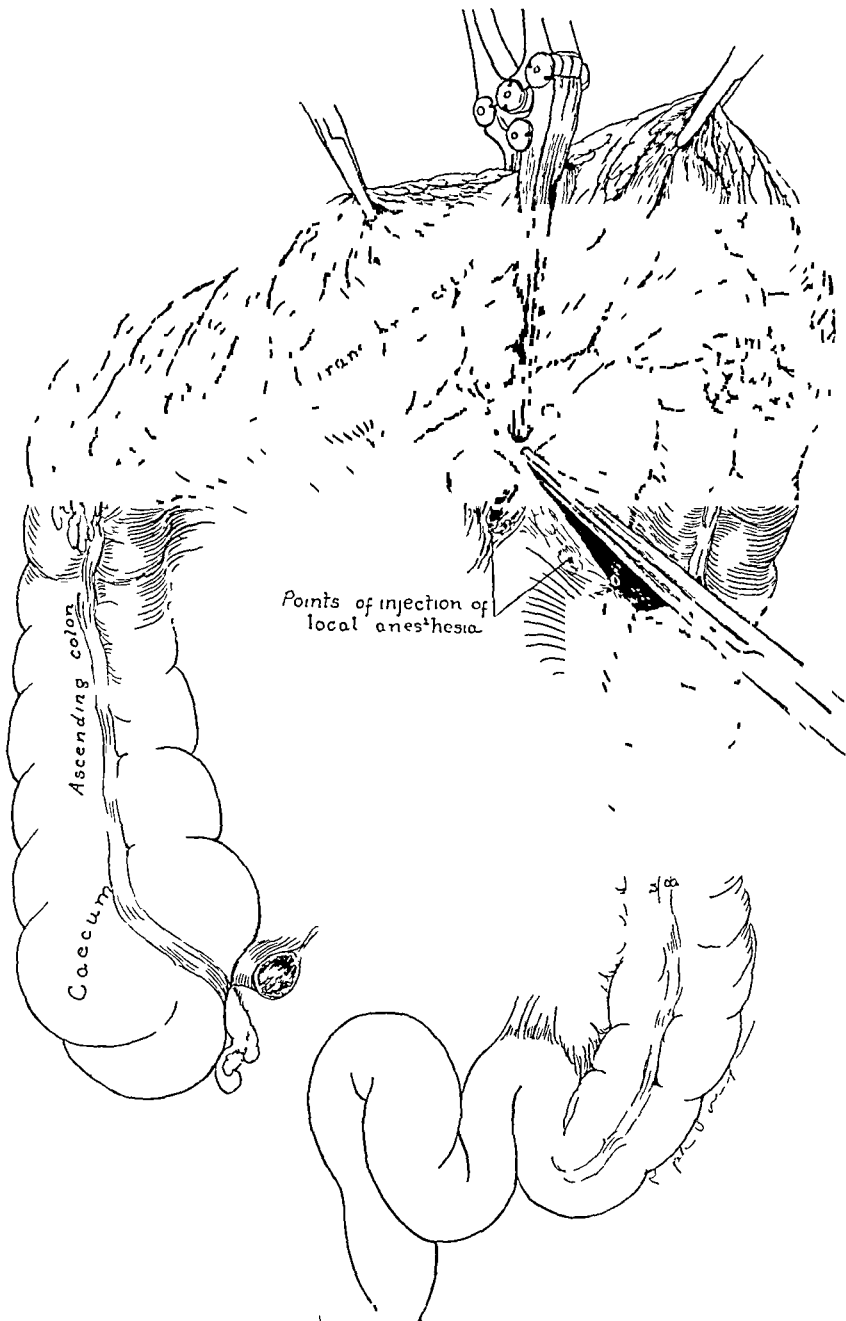


Fig 10—Resection of bowel segment by local infiltration of the mesentery

Preliminary ecctostomy (figs 7 and 8) followed by radical resection (figs 10 and 11) under regional anesthesia or spinal anesthesia supplemented by light ethylene (fig 9) is the procedure of choice.

In the descending and sigmoid colon a preliminary ecctostomy should be done in all cases in which obstruction is marked. Radical resection

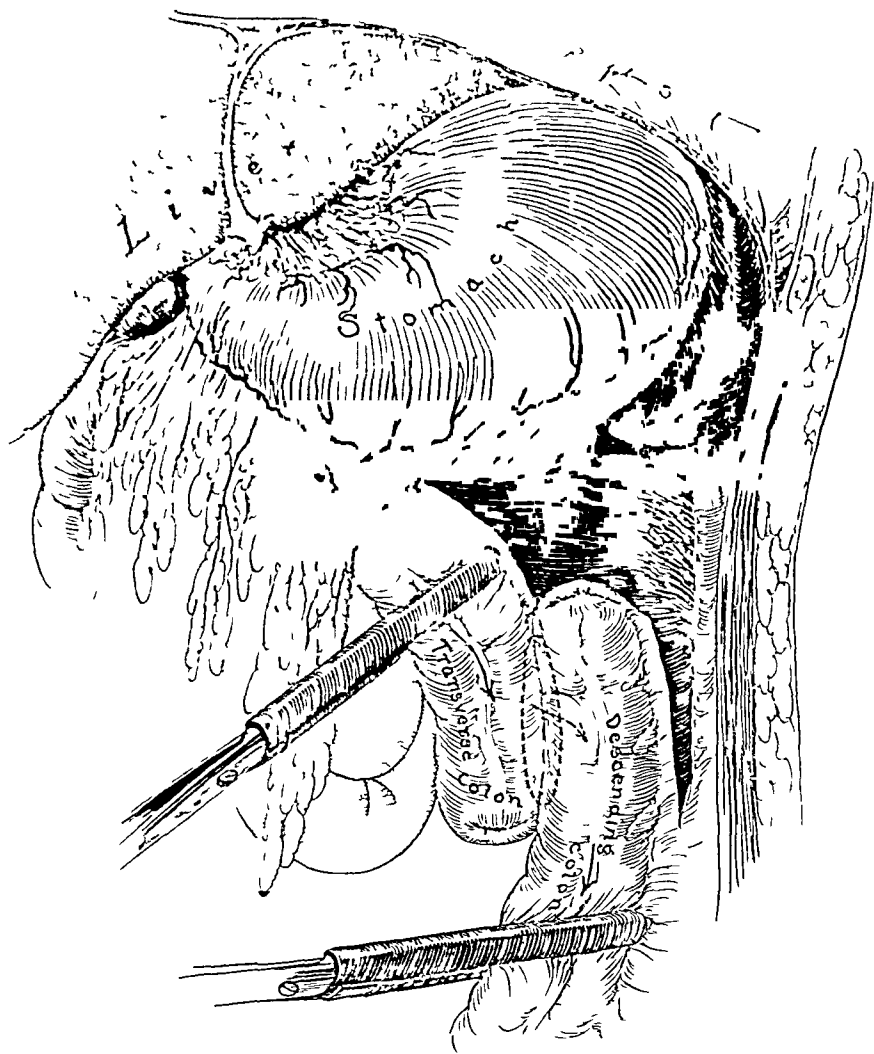


Fig 11—Lateral anastomosis of the transverse colon and descending colon following resection. Mobilization accomplished by splitting leaf of outer mesentery.

according to the closed technic as outlined in figure 6 is the preferable technic. Resection should be wide, as in C in figure 4, if glandular involvement is present.

As far as possible local, regional, spinal or ethylene anesthesia should be used.



## COMMENT

Nine cases of carcinoma of the colon, not including the rectum and sigmoid, have been selected for analysis as to the choice of operative procedure influencing the immediate and ultimate mortality. In a previous article I reviewed a group of cases of carcinoma of the rectum and sigmoid from a similar point of view.

The three M. B.'s are three of six brothers who have had resections of the cecum and ascending colon for carcinoma of the cecum.

*Analysis of Nine Cases*

Cases	Age	Type of Operation	Date of Operation	Location of Lesion	Grade of Malignancy	Results	Living	Type of Carcinoma
Mrs. W.	74	Cecostomy resection lateral anastomosis	1/ 5/27 2/ 5/27	Splenic flexure	II	Good	2 years	Adeno carcinoma
Mrs. L.	30	Resection lateral anastomosis	1/ 7/15	Transverse colon	IV	Good	4 years	Adeno carcinoma
Mrs. H.	58	Ileostomy	9/20/27	Cecum (marked obst.)	?	Died 24 hours	Died	/
Mr. B.	37	Resection cecum	9/12/27	Cecum	III plus	Good	1½ years	Adeno carcinoma
Mr. M.	43	Resection transverse colon and cholecystotomy	5/17/23	Transverse colon (marked obst.)	III	Died 3 days	Died	Colloid carcinoma
Mr. F.	77	Cecostomy resection lateral anastomosis	5/14/27 5/23/27	Upper descending colon	III	Good	2 years	Adeno carcinoma
Mr. T.	40	Resection transverse colon	5/12/24	Transverse colon with involvement of duodenum	III	Died 1/19/25 recurrence in liver	Died	Adeno carcinoma
Mr. B.	52	Resection cecum and hepatic flexure	5/27/28	Cecum	IV	Good	2 weeks	Adeno carcinoma
Mr. B.	43	Resection cecum abdomino-perineal	6/20/22 8/23/23	Cecum Recto sigmoid	III II	Good Good	7 years 1 year	Adeno carcinoma Adeno carcinoma

Patient 9 developed a carcinoma of the rectum seven years after the resection of the cecum and has had an abdominoperineal operation for radical cure. Another brother has a marked diverticulitis of the cecum and sigmoid at the present time.

This family group illustrates the marked inherited susceptibility to the development of carcinoma. The instability of the patient's tissue for further development of carcinoma is illustrated in patient 9, who developed the rectal neoplasm seven years later. An additional case is cited from the records of a woman who had a grade III carcinoma of the breast removed and who two years later developed a carcinoma of the rectum.

Mrs W. and Mr F. illustrate the old debilitated obstructed groups who require cecostomy and lengthy preparation for resection, the resection being done in these cases entirely under regional anesthesia.

Postoperative irradiation in all cases of cancer of the large bowel and rectum is considered an essential routine in the prevention of recurrence. It is felt that the good results obtained in the prolongation of life in the cases in which the patients had a grade III and IV carcinoma is due in a measure to deep therapy.

#### SUMMARY

The most important principles to be stressed are: 1. Relief from obstruction and cleansing of the bowel preoperatively and postoperatively should be done for relief from toxemia. Old and debilitated patients have poor healing powers. Gaseous distention from partial ileus and local peritonitis separates poorly healed suture lines in numerous cases. The safest procedure as a routine is that of a supplementary ileostomy when primary resection of the cecum, hepatic flexure or transverse colon has been done, if obstruction exists. Preliminary cecostomy or ileostomy at the time of radical resection or previously should be instituted when dealing with carcinoma of the splenic, descending or sigmoid colon, depending on the degree of obstruction and debility. It is possible to do primary resections of the large bowel when the patient is in good physical condition and mildly obstructed without ileostomy or cecostomy if sufficient bowel cleansing preparation has been previously instituted and obstruction relieved. Preliminary preparation with excess of fluids and nonresidue diet should be followed as a routine.

2. Careful attention to the blood supply of the bowel stumps before anastomosis is begun will avoid subsequent sloughing from lack of blood supply. If possible, resections should be planned according to the blood supply shown in figure 4, with the lymphatic supply illustrated in figures 1 and 2, in mind. The anastomosed segments should be mobilized so that all tension is avoided.

3. Preoperative preparation in regard to the restoration of water balance, medical therapy directed to the improvement of impaired kidneys and damaged cardiovascular system, correction of anemia and inanition are factors of vital importance for a successful outcome of a radical surgical procedure.

4. The operation of Mikulicz should be abandoned owing to the length of hospitalization, high percentage of recurrence, danger of thrombosis in vessels and postoperative herniation. The operative risk is not greater than that of a cecostomy followed by radical resection. It should be used only as an emergency procedure in case of gangrene of the bowel at the time of the primary operation.

5. Postoperative deep therapy should be done as a routine.

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# HYPERTONICITY WITH HYPERTROPHY OF THE PYLORUS IN ADULTS

## SURGICAL ASPECTS \*

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It is my purpose to call attention to a syndrome that seems to constitute a definite clinical entity, but one that the clinician seldom if ever takes into consideration when confronted with a patient who complains of discomfort in the upper part of the abdomen. It was brought to my attention by three patients who were seen recently at the University of Virginia Hospital. In each instance roentgenologic studies of the gastro-intestinal tract were made, and in all of them rather characteristic changes in the pylorus were noted. The roentgenologic observations will be reported in detail elsewhere by Archer<sup>1</sup>. Exploration of the abdomen revealed almost identical changes in each case, namely, hypertonicity and hypertrophy of the pylorus with narrowing of its lumen.

## REPORT OF CASES

CASE 1—C D, a white man, aged 63, was admitted to the medical service on Jan 5, 1926. Except for the fact that his father died of "cancer of the liver," the family and past histories were unimportant. The chief complaint was soreness in the upper part of the abdomen, which had first been noticed five months previously. There had been little real pain, but the discomfort had been constant and accompanied by the sensation of a "lump" in the epigastrium. There had been no apparent relationship between the discomfort and the taking of food. Nothing had relieved the symptoms. Nausea and vomiting had occurred on several occasions, but there had been no hematemesis and no melena. The patient had lost 25 pounds (11.3 Kg).

Examination revealed the patient to be somewhat undernourished. All of his teeth had been extracted. The heart and lungs were normal. There was some tenderness and rigidity of the upper portion of the rectus muscle on the right side, but no mass was palpable. The temperature, pulse rate and respirations were normal. The urine and blood did not show any abnormality, and the Wassermann reaction was negative. The systolic blood pressure was 126 and the diastolic 78. Analysis of 90 cc of brownish material withdrawn from the stomach showed no free hydrochloric acid, but blood, lactic acid and bacilli. Oppler-Bors were present. A roentgenologic study of the stomach revealed a constant but regular narrowing of the pyloric ring that appeared to be about an inch in width.

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From the Department of Surgery and Gynecology, University of Virginia

1 Archer, V W. Hypertrophic Pyloric Stenosis in Adults. Roentgen-Ray Aspects, Thesis submitted to the American Roentgen-Ray Society

It was thought that the patient had an early and operable case of gastric carcinoma and operation was advised.

Operation was performed under ether anesthesia by Dr. S. H. Watts. A rather elastic mass about 3 cm. in diameter was found in the region of the pylorus. The mass consisted of a greatly hypertrophied pyloric ring the muscle of which was quite spastic. The stomach, duodenum, gallbladder, pancreas and appendix were normal. The pylorus was incised longitudinally and closed transversely in order to increase the size of its lumen. Postoperative convalescence was uneventful. A letter received from the patient's physician March 10, 1929, more than three years after the operation, stated that he was in good health free from discomfort and had regained his normal weight soon after returning home.

CASE 2—C. T., a colored man aged 42, was admitted to the surgical service on March 19, 1928. His family history was unimportant. He had been operated on at this hospital in 1916 for hemorrhoids and again in 1922 for chronic appendicitis. At that time the observations made on roentgenologic examination of the stomach were identical with those to be described. The operator reported that there was no palpable abnormality of the stomach at that time. The appendectomy had relieved the symptoms for only a few months.

The chief complaint was soreness and discomfort in the upper part of the abdomen of six months' duration. There had been continuous soreness in the epigastrium but no real pain. A vague generalized abdominal discomfort had been noticed intermittently for a period of six years. There had seemed to be no constant relationship between the soreness and the ingestion of food. There had been no nausea or vomiting, no hematemesis and no melena. The patient had suffered with moderate constipation since 1922, before the appendectomy.

He was well nourished and his teeth seemed to be in fairly good condition. The heart and lungs were normal, but the abdomen was moderately tender and somewhat resistant in its upper portion particularly on the right side. The temperature, pulse rate, respirations and blood pressure were normal. Examination of the urine and blood did not reveal any abnormalities, and the Wassermann reaction was negative. Gastric analysis showed hyperacidity of a moderate degree. Roentgenologic examination of the stomach revealed a tubelike, spastic pylorus with constant spasm of the prepyloric portion of the stomach. The probable presence of a small gastric ulcer was reported.

I performed the operation under ether anesthesia, and exploration revealed a normal gallbladder, stomach and duodenum. The appendix had been removed, and there were no adhesions in the region. To make sure that no gastric or duodenal ulcer had been overlooked the stomach was incised, and the gastric and duodenal mucosa were inspected. The only positive observation was a definitely thickened and spastic pylorus which was not seen to relax at any time, and which offered considerable resistance to digital dilation. No further operative procedure was done.

Postoperative convalescence was uneventful and the patient left the hospital after two weeks. He returned on November 19 and stated that following operation he had been entirely free from discomfort for four or five months, but that later the discomfort had gradually returned. Cholecystographic examination did not reveal any evidence of cholecystic abnormality, and a roentgenologic study of the stomach did not show any change in the pylorus since the former examination. Small frequent meals were prescribed and apparently have relieved the patient for the present.

CASE 3—A. L. J., an unmarried white woman aged 39, was admitted to the medical service on April 17, 1928. The family history was unimportant. The

uterus had been suspended fifteen years before. The patient had never been able to eat large meals, because her stomach had seemed to fill quickly. Her chief complaint was of periodic attacks of pain in the epigastrium, which had troubled her for fifteen months. The pain had occurred soon after the ingestion of a meal. Sodium bicarbonate had afforded relief, and sometimes there had been relief after the ingestion of more food. Three weeks prior to the time of admission, the symptoms had become more severe and had frequently been accompanied by attacks of vomiting. At the time of examination, the patient had been unable to retain any food for a period of six days. There had been no hematemesis or melena. She had lost 30 pounds (13.6 Kg.)

At examination the patient appeared undernourished, quite intelligent and cooperative. There was some dental caries present. The heart and lungs were normal. There was tenderness and some muscle spasm in the epigastrium, and the upper right quadrant of the abdomen. The temperature, the pulse rate, respirations and blood pressure were normal. Examination of the urine, blood, stools and gastric contents did not reveal any abnormality. Roentgenologic examination of the stomach revealed a tubelike and spastic pylorus with a constant deformity of the lesser curvature just proximal to the pylorus. Six hours later, there was a residuum in the stomach estimated at 25 per cent. Gastric ulcer with pyloric obstruction was suspected, and, after dehydration had been combated by fluids given intravenously, operation was advised.

At operation, a spastic and definitely thickened pylorus was discovered. The stomach, duodenum, gallbladder and appendix seemed normal. The anterior two thirds of the pyloric ring and some of the contiguous stomach and duodenum were excised. Inspection of the stomach and duodenum did not reveal any evidence of ulceration. The opening was closed transversely, a funnel-shaped communication between the stomach and duodenum being left. Examination of the excised tissue showed some hypertrophy, cellular infiltration and edema of the muscularis.

The postoperative course was entirely uneventful, and the patient was discharged after two weeks. Later some diseased teeth were removed. When seen six months after operation, the patient reported a gain of 30 pounds (13.6 Kg.). She was seen again after an additional period of six months, and at that time reported that her health was excellent and that she was entirely free from abdominal complaint.

#### LITERATURE

Because the condition encountered in these patients seemed uncommon, I examined several textbooks and other literature dealing with gastro-intestinal disease, but I found relatively few and rather unsatisfactory references to dysfunctions of the pylorus in adults. Hypertrophic pyloric stenosis of congenital occurrence in infants was discussed frequently. Numerous data of anatomic and physiologic studies of the pylorus were found.

The anatomic location and structure of the pylorus are such that it plays an important rôle in the digestive processes of the stomach and upper part of the intestinal tract. It is a sphincter-like ring of circularly arranged muscle fibers at the outlet of the stomach. By the reconstruction and study of serial sections, Horton<sup>2</sup> showed that there

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<sup>2</sup> Horton, B. T. Pyloric Musculature with Special Reference to Pyloric Block, *Am J Anat* **41** 141, 1928.

is a sharp break in the circular fibers of the pylorus when it reaches the duodenum but that there is continuity of about one fourth of the longitudinal fibers from pars pylorica to duodenum by which the dilator muscle of the pylorus is formed

The mechanism by which the pylorus opens and closes has not been fully explained. The theory of complete control by acid and alkali has been found inadequate. In regard to nervous control McCrea and Brandt<sup>3</sup> have shown that the pylorus and duodenum get their nerve supply from a large branch of the vagus leading directly from the region of the cardia to the liver. That nerve fibers from both the sympathetic and the parasympathetic systems supply the pylorus is certain but which is constrictor and which inhibitory is not agreed on by investigators. Martin and Burden<sup>4</sup> reviewed recent experimental data on the subject.

Pyloric stenosis may be secondary to a condition such as peptic ulcer or gastric carcinoma or it may be primary. Primary stenosis may be caused by dysfunction or by changes in the musculature or by a combination of the two. Luminal narrowing of the pylorus due solely to dysfunction was called 'pyloric achalasia' by Hurst<sup>5</sup> who used the term to denote persistent failure of a sphincter to open widely in response to that coordinating mechanism by which visceral contents are alternately retained and expelled. Martin and Burden<sup>4</sup> and Deaver and Burden<sup>6</sup> in recent studies of such cases described a rational surgical treatment.

Stenosis of the pylorus due solely to changes in the musculature such as fibrosis and hypertrophy, probably is rare. Stenosis due to a combination of functional and structural causes seems to be the most probable type. Hypertrophic pyloric stenosis of congenital occurrence in infants is a common variety. The first description of this condition is attributed by Osler to Beardsley<sup>7</sup> (1788). Hirschsprung's<sup>8</sup> publication (1887) again directed attention to this condition. Downes<sup>9</sup> is responsible for comprehensive later studies of the surgical problem.

3 McCrea and Brandt quoted by Mayo C. H. Division of the Vagus for Pylorospasm, Proc. Staff Meet. Mayo Clin. **3** 177, 1928.

4 Martin E., and Burden V. G. Pyloric Achalasia and Peptic Ulcer. Ann Surg. **88** 565, 1928.

5 Hurst, A. F. The Sphincters of the Alimentary Canal and Their Clinical Significance. Brit. M. J. **1** 145, 1925.

6 Deaver, J. B., and Burden V. G. The Surgery of Pylorospasm. Ann Surg. **90** 530, 1929.

7 Beardsley Hezekiah quoted by Osler William, and McCrea Thomas. The Principles and Practice of Medicine. New York: D. Appleton Company, 1919.

8 Hirschsprung, quoted by Osler.

9 Downes, W. A. The Operative Treatment of Pyloric Obstruction in Infants. Surg. Gynec. Obst. **22** 251, 1916.



An interesting conception of the pyloric tumor in such cases was mentioned recently by Freeman<sup>10</sup>. He suggested that it may represent a reversion to ancestral type. In support of his hypothesis, he stated that the gizzard of granivorous birds is situated in the pyloric region, and that in some higher mammals, notably the colored anteater, the outlet of the stomach is occupied by a heavy muscular tumor in the same situation as the tumor found in cases with hypertrophic pyloric stenosis.

That primary stenosis of the pylorus with hypertrophy might occur in adults seems to have been recognized first by Maier<sup>11</sup>. He reported necropsies of twenty-one subjects varying in age from 12 to 75 years, and in each case there was hypertrophy of the pylorus.

Maylard<sup>12</sup> described seven cases in which he operated because of symptoms that suggested peptic ulcer, but instead of ulcer he found stenosis of the pylorus. Gastro-enterostomy relieved the symptoms in each case.

Mayo-Robson and Moynihan<sup>13</sup> quoted Maier<sup>11</sup> and referred to a case of Hussey's<sup>14</sup> in which gastro-enterostomy relieved the patient. They described a case of their own in a man, aged 24, in whom symptoms of gastric retention had progressed insidiously for five years. Exploration revealed a tightly contracted pylorus. It was dilated manually, and the patient had no further trouble for three months. At the end of that time, the symptoms recurred. Another operation was advised, and at that time a gastro-enterostomy was made, which gave permanent relief.

Bastianelli<sup>15</sup> described four cases in which there was pylorospasm but no retention of gastric chyme. Exploration showed thickening of the pylorus with slight evidence of a low grade inflammation but no ulceration. The Rammstedt operation was employed successfully.

Bianchetti<sup>16</sup> recorded a case in which he resected a thick pylorus which seemed to be malignant. Microscopic examination of the specimen, however, revealed only marked hypertrophy of the circular muscle.

10 Freeman, Leonard. Discussion. *Ann Surg* **90** 540, 1929.

11 Maier, R. *Beitrag zur angeborenen Pylorus stenosis*, *Virchows Arch f path Anat* **102** 413, 1885, quoted by Maylard (footnote 12).

12 Maylard, A. E. *Congenital Narrowness of the Pyloric Orifice a Cause of Chronic Gastric Disease in the Adult*, *Brit M J* **1** 416, 1904, **1** 626, 1920.

13 Mayo-Robson, A. W., and Moynihan, B. G. A. *Diseases of the Stomach and Their Surgical Treatment*. New York, William Wood & Company, 1904, p. 522.

14 Hussey, quoted by Mayo-Robson and Moynihan (footnote 13).

15 Bastianelli, R. *Pylorus Spasm and Its Surgical Treatment*, *Ann Surg* **81** 45, 1925.

16 Bianchetti, C. F. *Contributo allo studio della stenosi pilorica ipertrofica idiopatica dell'adulto*, *Arch ital di chir* **15** 585, 1926.

fibers, which he called "circular myoma" Crohn<sup>17</sup> reported one case in which a Rammstedt operation was used successfully, and Chaney<sup>18</sup> described another in which a Horsley pyloroplasty gave satisfactory results. Martin and Burden,<sup>4</sup> in reporting cases of pyloric achalasia called attention to the frequency with which the symptoms of achalasia simulated those of peptic ulcer, particularly the early stage of ulcer.

#### COMMENT

The pathogenesis of hypertrophic pyloric stenosis in adults is an interesting subject for conjecture. There are two possible origins, namely, it may arise *de novo* in entirely normal persons or it may represent activation of a previously quiescent but already hypertrophied or spastic pylorus. Clinically there are varying degrees of congenital hypertrophic pyloric stenosis, and it does not seem unreasonable to suppose that there may be so little stenosis in some infants at birth that they may pass through infancy, childhood and a part of adult life without trouble. Something in the intrinsic or nervous mechanism of the pylorus goes wrong, and symptoms appear.

Stenosis of the pylorus arising *de novo* in a previously normal person with a properly functioning pylorus seems improbable and difficult to explain on any basis other than that of imbalance of the autonomic nervous system. It is possible, however, that abnormal nervous stimuli or an abnormal response to stimuli may cause pylorospasm and that a long continued spasm may cause hypertrophy. Because of the incompleteness of the data on the subject, however, it is difficult to discover the etiology in each case.

The diagnosis of the condition should not present great difficulties. Were it borne in mind and considered more frequently when patients are examined who complain of vague or atypical symptoms in the upper part of the abdomen, fewer cases would go unrecognized. The frequency with which the symptoms resemble those of peptic ulcer, particularly the early stage of ulcer, has already been mentioned. One of my cases falls in this category, the other two patients complained of relatively constant discomfort and soreness rather than of actual pain in the epigastrium. There was an accompanying sensation of fulness. Two of the patients complained of nausea and vomiting periodically, and two had lost from 25 to 30 pounds (from 113 to 136 Kg). Physical examination did not reveal any typical changes.

The final diagnosis must be made roentgenologically. Constant spasm of the pylorus with more or less lengthening and narrowing of

17 Crohn, B. B. Congenital Pyloric Stenosis in Adult Life, *I. A. M. A.* 90:197 (Jan. 21) 1928.

18 Chaney, R. H. Congenital Pyloric Stenosis in Adult Life, *I. M. A. Georgia* 17:57, 1928.

the lumen of the pylorus is presumptive evidence, and when accompanied by signs of gastric stasis or retention is conclusive evidence of the presence of pyloric stenosis. That gastric stasis is not a constant feature of such cases, however, was stressed by Bastianelli. The degree of hypertrophy may be difficult to determine but is not in itself of major importance. It seems probable that in the past many of these cases have been diagnosed "pylorospasm," and dismissed as neurasthenic cases.

The treatment prescribed must depend on the severity of the syndrome and the degree to which the patient suffers discomfort and incapacity. In all except the mildest cases, in which antispasmodics and small, frequent meals might be given a trial, surgical treatment seems to be indicated. In my cases, one patient was treated by manual dilation of the pyloric sphincter. As in the case cited by Mayo-Robson and Moynihan, temporary relief from symptoms ensued, but the original discomfort recurred after a few months. In the other two cases, plastic operations on the pylorus were performed, and were followed by complete and permanent relief. The importance of prompt surgical treatment in such cases is suggested by the evidence of inflammation which is present in the tissues about the pylorus under these circumstances. That spasm of the pylorus may be of etiologic significance in the formation of peptic ulcer has been suggested already by others and myself.

The type of operative procedure to be employed is probably more a matter of personal choice than anything else. The Rammstedt, Heineke-Mikulicz, Judd, Horsley or Martin-Burden type of plastic reconstruction of the pylorus may be used to advantage. There is much to be said, however, in favor of the operation by which the major portion of the pyloric ring is actually excised, and parts of the adjacent stomach and duodenum are interposed between the severed ends of the sphincter. This type of operation leaves a funnel-shaped communication between the stomach and the duodenum with the minimum possibility of subsequent cicatricial constriction.

#### SUMMARY

I have called attention to a syndrome that seems to constitute a rather definite clinical entity. It is characterized by hypertonicity and hypertrophy of the pylorus with narrowing of its lumen, as was illustrated by the histories of the three cases reported. After a brief survey of the rather small amount of literature on the subject, these cases were discussed from the standpoint of the pathogenesis, diagnosis and treatment. A plea is made for the recognition of this condition and its consideration in the diagnosis of all vague or atypical symptoms referable to the upper part of the abdomen. The final diagnosis must be made roentgenologically, and the importance of surgical treatment and the types of operations to be used are referred to briefly.

# CHRONIC CYSTIC MASTITIS

PRELIMINARY REPORT ON THE NATURE OF THE PROCESS<sup>2</sup>

I STEWART RODMAN, M D

IN COLLABORATION WITH HELEN INGIFY, M D

PHILADELPHIA

Ten years ago in a paper<sup>1</sup> read before the surgical section of the Southern Medical Association, I made certain dogmatic statements concerning chronic cystic mastitis and other, as I then believed, definitely precancerous lesions of the breast. One of the penalties of increased experience is often that one can no longer be quite so sure, and so it is with our present-day belief concerning the nature of this process called by many names but perhaps most often, chronic cystic mastitis. The main issue is now what it was then—an appreciation of the importance of this condition with relation to its malignant tendencies.

I do not believe that my own experience with due regard for that of others, entitles me any longer to look on this process as definitely precancerous, as I thought it was ten years ago, and in fact until recently. That it does at times lead to carcinoma there can be no question, but, it does not do so nearly as often as was formerly thought. I cannot feel, therefore, that the surgeon is justified in doing the radical operation for this condition with the same security of belief that in so doing he is forestalling the development of cancer. There can be no doubt that many breasts have been needlessly excised because of this belief. The difficulty, however, lies in the fact that some of the cases become malignant, and it is impossible to say with any certainty which ones will do so. One must therefore be guided entirely by the case at hand and not by a set of rules. One must not be too much influenced by the specter of cancer in the offing. If each case of breast irregularity with respect to age, menstrual and sexual history, together with what is now known of the physiologic cycle of breast tissue behavior, is carefully considered, one can usually decide on the best procedure for that given case. The most important of these factors in women of child-bearing age is the menstrual function. The amount of involution and evolution which the breast undergoes during its active life is great, no other organ being given to more epithelial unrest.

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\* Read before the Section on Surgery at the Eightieth Annual Session of the American Medical Association Portland, Ore. July 10 1929

<sup>1</sup> Rodman, J Stewart. Pre-Cancerous Lesions of the Breast with Special Reference to Chronic Cystic Mastitis, South M J 13 348 (May) 1920

It is, of course, impossible to understand the pathologic changes in an organ if one fails fully to appreciate its physiology. The mammary gland, as is now known, is similar in the two sexes up to the age of puberty, but from then on fulfils its real function only in the female. These astonishing epithelial and fibrous tissue aggressions and regressions occur only in women and at times give rise to great difficulty in deciding between the normal and the abnormal.

We now believe that when this normal involuntary cycle in the breast is interfered with, disease begins, and that adenoma, fibroadenoma, papillary cyst adenoma, chronic cystic mastitis and even carcinoma may develop. It is, in reality then, one process with variations of the theme.

My continued interest in this subject clinically has given me the opportunity of seeing tumors of the breasts entirely disappear, which were not operated on because of a growing conservatism. This is a dangerous doctrine unless one has had a reasonably large experience in the matter, because valuable time might be lost in doing the radical operation to forestall the development of, or to attempt to cure a case of, early cancer. The surgeon must work hand in glove with a competent pathologist who has a special interest in the subject.

Recent literature justifies one in more conservative practice than that to which surgeons have been accustomed in the past. As long ago as 1907, Hitschmann and Adler<sup>2</sup> described the endometrium in the different stages of the menstrual cycle and thus threw new light on lesions of the uterus. It is known that these changes are correlated with the development and the regression of the corpus luteum. This work has a definite analogy to physiologic changes in the breast tissue as was shown in 1922, by Rosenberg,<sup>3</sup> who found in cut sections of the breast and the uterus, in cases coming to autopsy, a similar sexual cycle in the mammary gland. Polano and Sedening confirmed these observations in cases from the surgical clinic, but they denied that postmenstrual regression is always complete. Cheattle,<sup>4</sup> McFarland<sup>5</sup> and others have shown that what has

2 Hitschmann and Adler. *Wien med Wchnschr* 57 1297, 1907, *Monatschr f Geburtsh u Gynak* 27 1, 1908, *Arch f Gynak* 2 233, 1913.

3 Rosenberg, A. *History of Breast During Normal or Disordered Menstruation*, *Virchows Arch f path Anat* 262 298, 1926.

4 Cheattle, G. *Lenthal. Cysts and Primary Cancer in Cysts of the Breast*, *Brit J Surg* 8 149, 1920, *Benign and Malignant Changes in Duct Epithelium of the Breast*, *ibid* 8 285, 1921, *Cancer of the Breast*, *Brit M J* 1 869 (June) 1922, *Hyperplasia of Epithelial and Connective Tissue in the Breast. Its Relation to Fibroadenoma and Other Pathological Conditions*, *Brit J Surg* 10 436, 1923, *Desquamative and Dysgenetic and Epithelial Hyperplasias in the Breast*, *ibid* 13 509, 1926, *Early and Late Carcinoma of the Breast*, *Practitioner* 116 281 (April) 1926, 337 (May) 1926, *Chronic Mastitis, Cysto-Adenoma and Adenoma of the Breast*, *Arch Surg* 17 535 (Oct) 1928.

5 McFarland, Joseph. *Adenofibroma and Fibro-Adenoma of Female Breast*, *Surg Gynec Obst* 45 729 (Dec) 1927.

been considered a pathologic process is in reality probably nothing more than aberrant physiology

I have succeeded in enlisting the interest of my colleague, Dr. Helen Ingleby, Professor of Pathology at the Woman's Medical College, in this subject and the pathologic data in some of my recent cases are hers. I have labeled this a preliminary report, because time has not permitted a careful search of all of my past cases from this point of view. I feel justified, however, in the light of what has been written and of what a review of some recent cases has shown in making these statements at this time, realizing that in so doing I am going back on my printed words of the past but one is justified at times in changing one's mind, even in scientific matters.

Although the subject is chronic cystic mastitis, I believe that no adequate discussion of the subject can be entered into without first briefly considering some of the more recent additions to physiologic knowledge of the cycle of the mammary gland, as well as other variations from the normal, such as adenoma, adenofibroma, fibro-adenoma and papillary cyst adenoma.

Somewhere between the menstrual cycles the breast is in its resting stage, probably from the fifth to the fifteenth day after the last menses. At this time the fibrous stroma predominates the epithelial elements are only ducts and occasional acini. In old women and obese young women fat is also present. The ducts are lined by two layers of cells, an inner layer of cuboidal or columnar with nuclei that are small and stain deeply, and the basal cells that are smaller, and tend to be flattened. As the next menstrual period approaches, the cells become larger until they divide and new ductules are formed branching out from the old ducts like twigs on a tree. The epithelial border around the lumen becomes somewhat jagged and irregular, a change similar to that seen in the glands of the premenstrual endometrium. Meanwhile the surrounding fibrous tissue also softens, undergoing myxomatous and hyaline degeneration so as to allow for the expansion of the ducts. Lobules are thus formed which do not appear in the resting breast. The lining epithelial cells swell, the protoplasm becomes vacuolated and the nucleus is rounder and paler. Similar changes take place in the cells of the basal layer. Secretion takes place into the ducts and, clinically, in many women the breasts become swollen and tender at this stage. This then, is the premenstrual phase, and about a day or two before the onset of the menstrual flow, involution begins. At this time the epithelium degenerates and is shed into the lumen of the ducts much the same as the superficial layers of the endometrium are cast off during menstruation. Under the microscope, it is seen that the architecture of the lobules has been lost and they have a curiously jumbled appearance.

One now sees degenerate epithelial cells, often varying in size and shape, intermingled with round cells and proliferating fibrous tissue. After the menses are over these degenerated epithelial cells are absorbed. The breast is now in the postmenstrual phase which is short, as in about five days after the menses the breast again enters the resting stage.

If pregnancy intervenes, lactation changes begin. The breast hypertrophies in the same way as it does in the menses, but to a much greater extent. Numerous new acini are now formed and the periductal fibrous tissue is pushed aside, and is no longer distinguishable from the perilobular connective tissue. It is here that the epithelial activity, of course, is at its height. After lactation is over involution occurs, hyperplasia ceases, secretion is absorbed and the empty acini collapse because of the pressure of the elastic tissue on their walls. Most of the acini disappear at this time but the gland never returns quite to the normal virgin state. Lactation hypertrophy, both of the fibrous and the epithelial elements, remains to some extent. After the menopause further involution occurs.

It is of prime importance that a surgeon have complete data of the menses and sexual life of the patient under treatment, as I have seen what enormous differences can be expected in the premenstrual, postmenstrual, resting, lactating, postlactating and senile breasts. The amount of new growth taking place in the mammary gland at each sexual cycle is astonishing. Premenstrual proliferation is much more rapid than carcinomatous growth. In all probability, a hormone from the anterior pituitary body controls the secretion from the graafian follicle and the corpus luteum of the ovary, which in turn controls the growth of breast tissue. Moszkowicz<sup>6</sup> believes that growth and regression during the sexual cycle in the breast can sometimes be traced to ovarian dysfunction, and that the ovaries exert a controlling influence over evolution and involution of the gland.

What aberrations might be expected if proper growth and involution were interfered with? Such interference might be local or generalized in the breast tissue. Either epithelium or fibrous tissues, or both, might take part in the aberrant process. It has been shown that local changes occur in the uterine mucosa when inadequate development of the graafian follicle causes a chronic but localized hyperplasia of the endometrium. Such a localized process in the uterus becomes a uterine polyp. I believe that chronic local hyperplasia in the breast results in an adenoma—adenofibroma if the epithelial elements are affected as well as the fibrous tissue, fibro-adenoma if the fibrous tissue predominates. If the epithelial cells come to a stage of secretion, and the normal absorption is for some

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6 Moszkowicz, L. Sexual Cycle, Mastopathy and Tumor Growths of Female Breast, *Arch f klin Chir* **144** 138, 1927, Cystic Disease of Breast as Precancerous Epithelial Proliferation, *Virchows Arch f path Anat* **262** 531, 1926

reason intertered with cysts of the acinar type will occur. It appears that cells shed normally into the lumen of the ducts in the postmenstrual phase, do not pass in large quantities from the nipple, as it is known that such a discharge during menstruation is rare. If the fibrous tissue was chiefly affected, the ducts would try to proliferate as they do normally in the premenstrual phase, but they would be pressed on and pulled out by the fibrous tissue, and result in the ordinary intracanalicular type of fibro-adenoma. If this process is carried further, the ducts become invaginated and there results a series of projections within the lumen of the cavity covered by epithelium. If the ducts are distended by unabsorbed secretion, the result is a papilloma.

One of the essentials of a benign tumor is that it must have a capsule. In many of McFarland's cases and in some of mine, careful pathologic examination did not reveal a true capsule, even though the surgeon felt that there was one at the time of its excision from the surrounding breast tissue. Many of the tumors are semi-encapsulated, showing complete continuity with a normal breast on one side and sharp demarcation from breast tissue on the other. In some of the cases of localized aberrant physiology, the proliferation of the fibrous and epithelial elements has been sufficiently great to push the surrounding fibrous tissue aside to form a capsule. If there is no attempt at localization and the same changes are widespread, one finds chronic cystic mastitis or the abnormal involution of Warren, which I now believe to be the best of the many names suggested. Moszkowicz has grouped the aberrant physiologic changes under the term 'mastopathy,' but I cannot believe that for clinical usage this term will find as much favor as that of Warren. It is true that some of these changes have to do with abnormal evolution rather than involution, but in the majority, involution is at fault. It is certainly a tribute to Warren's original observations on this disease made many years ago that, in my opinion at least, the name that he gave it is still the best.

There can be no doubt that carcinoma may develop in a breast showing abnormal involution. We do not believe now, however, that it happens nearly so frequently as we formerly thought, or that cause and effect have the same direct bearing. Carcinoma, however, when its origin can be traced, seems to arise in larger ducts, not in lobules, and we now believe that while this condition of abnormal involution may prepare the ground, so to speak, that in the vast majority of cases nothing further than the aberrant physiologic changes occur. Unfortunately, microscopic examination does not disclose whether a given lesion of the breast is carcinomatous or not, until it is advanced. Pathologists, I believe, agree that there is absolutely no way of recognizing a carcinoma cell other than by its behavior.



## CONCLUSIONS

1 The first essential in dealing with breast irregularities is a real appreciation of the astonishing amount of epithelial and fibrous changes that normally occur during the premenstrual, postmenstrual, lactation, postlactation, menopause and senile phases

2 During the active phases of the life cycle of the gland, it is necessary that one has accurate data concerning the time of the menstrual period, in its relation with the appearance and development of the tumor in question, as well as all other data which will put the case in point into one of the phases given

3 Conservatism is justifiable in dealing with abnormal involution, provided one fully appreciates the somewhat rare development of carcinoma in such cases. Any tumor that does not change with local treatment (support and mild counterirritation) after one menstrual period has been passed should be removed by local excision and submitted to a frozen section, the pathologist choosing the part to examine microscopically

5 If there is reasonable doubt in the mind of the pathologist who has made this subject one of special interest, after microscopic examination of the frozen section, the surgeon should proceed with the radical operation as for carcinoma

6 Regardless of the vast amount of interest which this subject has aroused in the past, considerably more evidence from experimental, detailed physiologic and pathologic sources is necessary before some of the statements made in this paper can be confirmed

## ABSTRACT OF DISCUSSION

DR. A. R. KILGORE, San Francisco. I have long felt that the cause of chronic cystic mastitis would be found bound up with internal gland hormone dysfunction. Chronic cystic mastitis (abnormal involution) can be divided into two quite distinct types in such a manner as to simplify the problem of its relation to cancer. The one universal characteristic of all stages and types of abnormal involution is an increase in the number of individual gland units. The first stage in the involution may be shown as a simple increase in number of acini, the lobules being larger than normal and closely packed. With dilatation to form cysts, the epithelial lining may react in two ways. It may either remain smooth and eventually become atrophied or entirely disappear, or the epithelium may be thrown into hyperplastic folds and eventually into a papilloma, composed of almost solid, atypical epithelium. Cancer would not be expected from atrophied or absent epithelium, and I believe it is now generally accepted that cancer occurs in connection with the smooth-walled cyst of the first type only as a rare incident. Cancer would not be unexpected, and, I believe, does arise from hyperplastic epithelium. In the laboratory at the San Francisco Hospital, there is a small group of thirty-five specimens of the nonhyperplastic type, none of which presented cancer at operation. There are nine more or less extensive tumors of the hyperplastic type (nonencapsulated cystadenoma) in four of which cancer had already developed at the time of opera-

tion. In three of these four cases the presence of cancer was proved by metastasis or by later known death caused by cancer. Cancer not being found at operation in one type and such a high proportion presenting cancer already developed in the second type strongly suggest that the hyperplastic type of abnormal involution is a definite precancerous condition.

DR J S HORSLEY, Richmond, Va. Dr Rodman's paper and Dr Kilgore's discussion have been illuminating, and have helped to clarify the subject of chronic cystic mastitis, which has been much confused and misinterpreted. To say, on the one hand, that there is no connection between chronic conditions such as this abnormal involution in which there is sometimes a distinct tendency toward hyperplasia of the epithelium and toward cancer, and, on the other hand, to say that certain types of abnormal involution, in which there is no hyperplasia of the epithelium, have a tendency to cancer, is illogical. One extreme is as bad as the other. One knows that in other regions of the body chronic processes, whether one calls them inflammatory or not, that are accompanied by a hyperplasia of the epithelium, tend toward malignant conditions in some instances. There are, of course, exceptions. For instance, primary cancer practically never develops on the soles or on the palms, even though the palms are subject to frequent trauma probably more than any other region of the body. It seems that this exception may be due to biologic reasons or to the fact that the two tissues have been subject to trauma in evolutionary times and have acquired a marked stability. After all, the cancer cell is the result of instability of the tissue, and of the inability of the tissue to control its constituent cells. When the stability is marked as in the palms and soles, no amount of trauma seems able to cause that chaotic condition which is cancer. In comparatively modern conditions, modern from a biologic standpoint, trauma, or chronic processes that appear to accompany civilization or result from it, frequently do not have the proper biologic corrective influence that is necessary to keep the cells within bound. I think it is undoubtedly true that, occasionally, there is cancer in connection with chronic cystic mastitis or abnormal involution. I have had one or two cases of my own which I think are quite definitely pathologically proved, but to do a radical operation in practically all of the cases is unnecessarily mutilating surgery. It seems to me that the grounds that have been recommended by Dr Rodman and suggested by Dr Kilgore are admirable.

DR J S RODMAN, Philadelphia. I am in entire agreement with Dr Kilgore and Dr Horsley, and wish to thank them for their discussion.

# A REVIEW OF UROLOGIC SURGERY

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## KIDNEY

*Anomalies*—Bagg<sup>1</sup> reported the results of experimental studies dealing with the effect of roentgen and radium treatment for certain congenital hereditary abnormalities of the genito-urinary organs that were found in laboratory animals. His data have been collected during the last six years and are based on records of 5,600 necropsies, especial attention having been given to selective breeding for renal defects. One thousand and fifty-seven animals had defects of the kidney. There were 1,000 animals, 519 males and 481 females, with one or both kidneys missing. One kidney was absent in 630 animals, and both kidneys were absent in 334 animals. Twenty-five animals had a solitary kidney which was reduced in size. Thirty-five animals had one hydronephrotic and one normal kidney. There were 11 animals with one hydronephrotic kidney, the other was not present. This summary also considered 17 animals in which one or both testes were abnormal. The elimination of a testis after birth has been traced to diffuse hemorrhagic extravasation within that organ, a condition which was noted a few hours after birth, and the same testis was missing at necropsy several months later.

Well marked anatomic abnormalities have appeared in the descendants of male and female mice that have been submitted to treatment with roentgen rays, the defects breed true, are recessive in character and behave mainly as mendelian in inheritance. These studies are of clinical significance in indicating that caution should be used in irradiation over the region of the ovaries when the patient is pregnant.

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<sup>1</sup> Bagg H J. Hereditary Congenital Anomalies of the Genito-Urinary Organs. *Am J Surg* 7:211 1929

This caution also applies to irradiation of the gonads in men when the product of these organs may enter into a pregnancy at some later date

Only the parent generation animals both males and females, were irradiated. The first type of abnormality to be found was the presence of congenital defects of the eye in certain of the unirradiated descendants in the third and subsequent generations. It has bred true for nineteen generations over a period of six years. In still later generations peculiar forms of defects of limbs made their appearance, clubbing, syndactylism, hypodactylism and polydactylism being the most prominent types. By selective breeding these abnormalities have also been intensified so that in certain litters as many as seven of eight young have shown one or more defective limbs.

The first type of defect of the kidney was noted when necropsy was performed on animals of the fifth generation that were descendants of the group that had been irradiated. Some of these animals had a so-called solitary kidney defect. By breeding males and females of this group, the relative frequency of incidence of this abnormality was raised from 16.75 per cent in unselected animals to 57 per cent in litters in which both parents had the solitary kidney defect.

*Stones*—Chwalla<sup>2</sup> reviewed 143 cases of renal stone and 91 of ureteral stone from the city hospital of Vienna. Sixty per cent occurred in men and 40 per cent in women. Substantiating Israel's observation there were twice as many ureteral stones in men and only 20 per cent more renal stones. Forty-one per cent were on the right side, 46 per cent on the left and 13.6 per cent were bilateral. Among the 55 cases of ureteral calculi in men, 65 per cent were in the pelvic portion of the ureter, 12.7 per cent in the iliac and lumbar portions and 9 per cent just below the renal pelvis. Among the stones in the lower part of the ureter, 19 were intramural and 15 were in juxtaposition to the bladder. Of the 26 cases of ureteral stone in women, 19 (73 per cent) were in the pelvic region, 2 (7.7 per cent) were in the iliac region and 5 (19 per cent) were in the upper part of the ureter. Stones were not observed in the lumbar region of the ureter. In 13.5 per cent of the cases the stones were multiple. Lithiasis is chiefly a disease of the third and fourth decades, and is sometimes observed in the first and seventh decades.

Chwalla concluded that the output of indigo carmine (sodium indigolindisulphose) does not give an accurate indication of the degree or extent of the pathologic process present. Even in markedly changed kidneys function may recover after removal of the stones. Large hydronephrotic kidneys (associated with stones) were noted to return

<sup>2</sup> Chwalla, Rudolf. Das Spätschicksal unserer Nieren- und Uretersteinfälle, *Ztschr. f. urol. Chir.* 26: 157, 1929.

to normal capacity after a period of years. Observations did not show that a kidney in this condition had any reflex or toxic influence on a normal kidney. In most cases, following pyelolithotomy, nephrolithotomy, pyelonephrolithotomy or ureterolithotomy, the indigo carmine output of the affected kidney is likely to become almost normal soon after operation. In cases in which this does not occur there is usually a recurrent stone or a remaining stone but seldom a badly injured kidney.

Recurrent or overlooked stones are the most common cause of the continuation of an infection following operation. Seventy-two and two-tenths per cent of the cases of renal stone and 70.2 per cent of the cases of ureteral stone were traced. In 31.75 per cent of the cases of ureteral stone there were definite signs of recurrent calculus on one side or the other. There was an incidence of recurrence in cases in which operation was performed or at least 8 per cent following pyelolithotomy, 36.3 per cent after nephrolithotomy and 7.4 per cent following ureterolithotomy. Following nephrectomy there was an incidence of 16.2 per cent of stones in the remaining kidney. These data show that there is an average of at least 18.5 per cent recurrence of stones.

[Compilers' Note—Much has been written recently on recurrence of renal stones. Cifuentes<sup>3</sup> found recurrence of stones in only 2 per cent of aseptic cases. Rosing<sup>4</sup> reported statistics relative to infection and recurrence. In 44 (40.3 per cent) of 109 cases of nephrolithotomy there was a recurrence, 58 were aseptic cases, of which only 15 (25.8 per cent) recurred. Nephrolithotomy was performed in 27 cases of infected urine, there was recurrence in 10 (37 per cent). In 19 (79 per cent) of 24 cases in which there were micro-organisms of decomposing urea there was recurrence. There were only 7 cases of pyelolithotomy, and in 2 of these the disease recurred. Sixty-eight per cent of all recurrences occur in infected kidneys. It is interesting to compare Rosing's figures with those in a series of cases reported by Braasch and Foulds<sup>5</sup>. Recurrence followed in 44 (11.8 per cent) of 375 cases after pyelolithotomy, 25 (24 per cent) of 104 cases after nephrolithotomy and 2 (4.1 per cent) of 48 cases after combined nephropyelolithotomy.

Rafin<sup>6</sup> reported a series of cases in which lithiasis recurred after pyelotomy in 23 per cent of the cases, after nephrotomy in 15 per cent and after primary nephrectomy in 3.3 per cent. In the combined series

3 Cifuentes III Sitzung Fernresultate der Operationen wegen Nephrolithiasis, Ztschr f urol Chir **16** 169, 1924

4 Rosing, C M Infection as Cause of Recurrence Following Operations for Kidney Stone, Acta chir Scandinav **57** 387, 1924

5 Braasch, W F, and Foulds, G S Postoperative Results of Nephrolithiasis, Tr Am A Gen-Urin Surg **16** 155, 1923

6 Rafin Valeur comparee des diverses interventions pour lithase renale, J d'urol **18** 523, 1924

lithiasis recurred after pyelotomy in from 0 to 25 per cent of the cases (aseptic) and in from 7 to 50 per cent of the cases (septic), after nephrotomy in from 32 to 17 per cent of the cases (aseptic), and in from 7 to 54 per cent of the cases (septic) and after nephrectomy in from 1 to 4 per cent of the cases ]

Thompson<sup>7</sup> studied necropsy records of 12,888 cases in order to review the question of the formation of stones in the kidney and ureter. In this series some lesion occurred in the urinary tract in 2,200. Calculus formed in 162 cases. The incidence of the formation of stone was approximately equal in the two sexes, especially during the first decade of life. From the ages of 11 to 40 lithiasis was more common among women than men but from the age of 41 its occurrence was greater in men. Stone is more commonly found on the right side than on the left in both sexes and is more commonly located in the pelvis or calices of the kidney than elsewhere in the urinary tract.

Thompson commented on what he termed "travelling stone," that is, a stone in the kidney which passes along the ureter and into the bladder, then through the urethra. Bearing in mind the data noted at necropsy he concluded that stones travel more frequently in women than in men and he noted in his clinical experience that a stone is impacted in the right ureter more commonly than in the left in men.

In a third of the cases the stones formed on both sides. Thompson did not give much credence to the idea that hypertrophy of the kidney on one side results in response to disease of the opposite side, and considered that this is less common than is generally thought. Stones may recur after operation for their removal, a condition usually due to careless or incomplete removal of the calcareous materials. In three cases the stone was associated with new growth and apparently was the causative factor in its formation.

Quinby<sup>8</sup> stated that unless there are external contraindications all renal calculi which are too large to pass through the normal channels should be removed surgically. The aim of such operation should be to remove the stone with as little destruction of renal tissue as possible, with free drainage of the kidney assured. Free mobilization of the kidney, together with the use of roentgenograms made at the operating table, makes it possible to cope with the problem presented in whatever way seems best. The simplest attack on the kidney is that of pyelotomy, the next in severity is pyelonephrotomy and the most severe is extensive nephrotomy. Nephrectomy should be performed only in cases

7 Thompson, A. R. Renal and Ureteric Stone Formation. *Guy's Hosp. Rep.* 79: 173, 1929.

8 Quinby, W. C. The Operative Treatment of Renal Lithiasis. *Am. J. Surg.* 7: 234, 1929.

in which the kidney has been rendered valueless by the disease. After all obvious concretions have been removed, further search by roentgen examination should be made in order to be sure that no particles remain to serve as the nucleus for subsequent formation of stone. Particles are best removed by washing and by the use of the negative pressure tube. A final roentgenogram should show the kidney entirely free from shadow-casting material. Patients should be closely observed after operation, and every effort should be made to restore the urinary passage to a sterile condition.

Graves<sup>9</sup> reported a case to illustrate the rapidity with which renal stones may develop in some cases. The patient, a man aged 29, complained of recent acute pain. Examination revealed a stone 1 by 0.5 cm in the middle of the left ureter, with incipient hydronephrosis above it. A roentgenogram also showed the shadow of a minute concretion apparently in the cortex of the kidney on the right side. Infection or other demonstrable abnormality of the urinary system was not present. The ureteral stone was removed. Eighteen months later, the patient returned with recurrent pain. Roentgenograms showed a large renal calculus on the left side, associated with several smaller stones. The urine from the left kidney was infected with *Staphylococcus aureus*. The small fragment of stone in the cortex of the right kidney had not changed in size and position as compared with the previous examination. Left nephrectomy was necessary because of the stones and the extensive infection throughout the organ. Convalescence was satisfactory.

[Compilers' Note—The question of the time necessary for the formation of urinary calculus has been debated by many urologists. Stones in the bladder occasionally arise rapidly, particularly when a foreign body such as a catheter or a suprapubic tube is present. Instances of formation of stone 4 or 5 cm in diameter have occurred over a period of from six to seven weeks, between the stages of prostatectomy. Cases have been reported of stones in the kidney growing to 1 cm in diameter in two months. In one case a stone was observed over a period of five years. At the onset it was 6 mm in diameter, five years later it completely filled the pelvis, with destruction of the kidney and marked reduction of function, necessitating nephrectomy.]

Eisendrath and Arens<sup>10</sup> considered the difficulty in distinguishing between shadows of biliary and renal calculi on account of the anatomic

9 Graves, R. C. Rapid Formation of Renal Calculus, *New England J. Med.* 200:421, 1929.

10 Eisendrath, D. N., and Arens, R. A. Pyelography and Cholecystography as Aids in the Differentiation of Shadows Due to Renal or Biliary Calculi, *Surg. Gynec. Obst.* 49:1, 1929.

proximity of the gallbladder and kidney in normal persons. The radiographic opacity of any calculus depends on the atomic weight of the constituents and the structure and thickness of the calculus. Soft calculi are much less opaque than hard calculi. The range of migration of biliary stones is usually greater than renal or ureteral calculi except in cases in which the latter have formed in a dilated renal pelvis or ureter or both. Cholecystography or pyelography or the combination of these two methods is a valuable diagnostic aid in distinguishing between biliary and renal stones. Eisendrath and Aliens make multiple exposures by rotating the patient, because in some instances the suspected calculus may appear to lie in the gallbladder or kidney, while in others its true position is at once evident.

The opacity of urinary calculi decreases according to the following: calcium carbonate, calcium oxalate, calcium phosphate, magnesium phosphate, uric acid and urate, cystine and xanthine and fibrin.

[Compilers' Note—With the advent of cholecystography came another method of differentiating shadows of renal and biliary origin. Eisendrath previously reported cases illustrative of the value of the combined use of the pyelogram and cholecystogram. As the shadow of the gallbladder and the pyelogram are found at times to overlap and to include the shadow of stone, the situation may still be confusing, thus the use of multiple exposures at different angles with rotation of the patient. Pyeloscopy or manipulation of the iodide-filled renal pelvis under the fluoroscope, as is being developed by Braasch, could probably be applied with value in some of these cases. One can at once see the importance of using both pyelography and cholecystography in conjunction when shadows in the upper right quadrant of the abdomen lead to confusion.]

*Tumor*—Plaut<sup>11</sup> reported the case of a woman who had had calculi in the renal pelvis, and in whom the epithelium of the pelvis and part of the ureter were cylindric. The epithelium of the mucous membrane formed glands which connected with an underlying stroma imitating the structure of the intestinal wall. At the same time the muscle tissue became hyperplastic. A portion of this probably originated from destroyed blood vessels and part from the wall of the renal pelvis or from the renal papillae. The influence of infection in this process cannot be determined. Renal atrophy resulted from the concerted pressure of the pus, mucus and tumor. Some of the tubules appeared to have regenerated, and there were areas similar to the renal blastoma.

11 Plaut, Alfred. Diffuses dickdarmähnliches Adenom des Nierenbeckens mit geschwulstartiger Wucherung von Gefässmuskulatur. *Ztschr. f. urol. Chir.* 26: 562, 1929.



The tumor described cannot be identified by the literature. It has some characteristics similar to exstrophy of the bladder. The similarity to intestinal structure must designate it as blastoma. Terms such as heteroplasia, protoplasia and metaplasia do not seem to explain the pathogenesis. The presence of the renal stone and the severe infection can scarcely be etiologic factors. To explain the diffuse extension through the ureter, pelvis and calices, multiple points of origin must be considered.

Hunt and Hager<sup>12</sup> reported that of 271 cases of malignant renal tumors in which the patients were operated on in the Mayo Clinic over a period of ten years, 241 were traced. In a group of 225 cases of adenocarcinoma, 199 were traced. In 177 nephrectomy had been performed and in 22, exploration. Of the 199 patients traced, only 73 are living, 62 were alive after three years, 37 after five years, and only 3 after ten years. There were 21 operative deaths. The presence of a palpable tumor was not found to influence the final result, unless the size produced difficulty in operations. Radiotherapy was given in many cases, but it was difficult to estimate whether benefit was derived from it.

There were 10 patients with sarcoma, 8 of whom were traced. The average age of the patients was 47 years. The tumors were large, and in the pyelograms it was difficult to distinguish between renal and extra-renal tumors. Nephrectomy was performed on 7 patients, only 2 of whom are alive. One was operated on two and a half years later for secondary growth, the other was healthy at the end of three years. Radiotherapy was given with no proved beneficial result.

Malignant tumors occurred in 13 children, 11 of whom were traced. The ages ranged from 20 months to 7 years. All had palpable tumors, 8 on the right side and 3 on the left. One patient is alive and healthy seven years later, and another two years later, with signs of recurrence. It was doubtful if radiotherapy affected the results.

Twenty-three patients had epithelioma of the pelvis. Of 12 patients traced, 8 had died. One lived as long as nine years.

[Compilers' Note.—The poor results of radiotherapy in dealing with any type of renal neoplasm, the ominous outlook for sarcomatous patients with any form of therapeutic attack, and the relatively bad prognosis for malignant renal tumors in children summarize the conclusions of these authors, which are in accord with the opinions of most investigators.]

The earlier the treatment is instituted, the more extensive the operation and the more the tumor corresponds to the type of adenocarcinoma

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<sup>12</sup> Hunt, V. C. and Hager, B. H. A Review of 271 Cases of Malignant Renal Neoplasms. *S. Clin. N. Amer.* 9: 149 (Feb.) 1929.

of hypernephroma the more the chance of cure by radical surgical procedures. As for degrees of malignancy the pure sarcoma and carcinoma usually rank first the mixed cells of Wilms' tumors seen in children next and last the hypernephroid types. The relatively better outlook in dealing with early epithelioma of the renal pelvis is shown by Hunt and Hager's cases.]

*Hydronephrosis*—Mezo<sup>13</sup> considered various methods of reconstructing hydronephrotic renal pelvis among which he mentioned plication ureteropelvic anastomosis and reimplantation. In a normal physiologic condition the ureter is inserted into the deepest portion of the pelvis while in hydronephrosis it is often inserted at a higher point. The object of the different operative measures is to repair so as to eliminate any residual urine in the renal pelvis. These operations rarely are successful even in uninfected cases. The formation of fistula or of perinephric abscess usually results and in many cases secondary nephrectomy becomes necessary.

In some cases "transversopenia" had aided in the treatment for the hydronephrosis. In this procedure the urinary tract is not disturbed, the kidney is suspended in a transverse position to the major and minor psoas muscles. This technic may eliminate pelvic retention and in many instances it saves the kidney.

MacMyn<sup>14</sup> stated that hydronephrosis and dilatation of the ureters in children does not occur frequently. It may be unsuspected and overlooked and rapidly cause death. The condition is marked by disorders of urination due to obstruction and to added infection. A valvular obstruction in the posterior urethra is more common than has been previously believed and is the cause of many cases of dilatation of the urinary tract heretofore attributed to other factors. The disease may be associated with other congenital abnormalities, whether in the urinary tract or elsewhere in the same child.

*Tuberculosis*—Dozsa<sup>15</sup> commented on the effect of pregnancy on renal tuberculosis and stated that it presented as serious an outlook to the pregnant woman as does pulmonary tuberculosis. Pregnancy has a deleterious effect on renal tuberculosis. A latent pulmonary process may become active and affect the kidneys, or the process being latent in the kidneys may become evident. He does not believe that there may be latent tuberculosis which may be activated by the pregnancy.

13 Mezo Bela: Transversopenia renis. Eine neue Methode zur Behandlung der Hydronephrose. *Ztschr. f. urol. Chir.* **26**: 488, 1929.

14 MacMyn, D. I.: On Dilatation of the Ureters and Hydronephrosis in Childhood, *Brit. J. Urol.* **1**: 150, 1929.

15 Dozsa Eugene: Nierentuberkulose und Gestation. *Ztschr. f. urol. Chir.* **25**: 310, 1928.

without having given previous symptoms. Clinically, the evidence seems to be that pregnancy may start a renal process just as it does a pulmonary one. Pregnancy may cause an extension of the tuberculous process in the kidney to the cavernous form and cause an added absorption of toxins to those which naturally accompany pregnancy and which are of great importance to mother and child. There are some cases on record in which the condition remained unchanged by pregnancy.

Nephrectomy is indicated if the process is unilateral. Interruption of pregnancy is not sufficient to arrest the process. In bilateral tuberculosis or tuberculosis of the remaining kidney, termination of the pregnancy is indicated, with conservative local treatment. Doza has observed that women on whom nephrectomy has been done go through pregnancy well.

[Compilers' Note—Pugh<sup>16</sup> recently reviewed the literature on the association of tuberculosis and pregnancy. He found that in 69 per cent of cases in which exacerbation of unilateral tuberculosis occurred during pregnancy, abortion or nephrectomy became necessary immediately. Instead of increasing the necessity for conservative treatment in renal tuberculosis, it seems that pregnancy contraindicates it. Interruption of pregnancy does not stop the tuberculous process, and this procedure is increasingly dangerous in later months. Pugh recommended nephrectomy in these cases. Pregnant women stand the operation well, and it is not more serious than when it is performed in the nongravid state.]

Mair<sup>17</sup> made a study of pregnancy in relationship to tuberculosis of the kidney and the bladder, to isolated tuberculosis of the kidney, to nephrectomy with continuing tuberculosis of the bladder and to tuberculosis in the normal bladder after nephrectomy. He observed that pregnancy aggravated the tuberculosis in each case, and in some instances a secondary infection from the colon bacillus took place. If complications arise, removal of the fetus may be necessary.

Wildbolz<sup>18</sup> has performed 660 nephrectomies for renal tuberculosis, with an operative mortality of from 2.2 to 2.5 per cent. In a series of 140 consecutive nephrectomies for renal tuberculosis he did not have any deaths. In tracing 341 of his patients from ten to twenty-one years after nephrectomy for renal tuberculosis he found that 40 per cent are dead. More than half of them died from tuberculosis of the remaining kidney or from pulmonary tuberculosis. The third most common cause of death was military tuberculosis. Fifty-nine per cent of the patients

16 Pugh, W. S. Tuberculosis of the Kidney in Pregnancy, *Ann Surg* **86** 591, 1927.

17 Mair, H. Schwangerschaft und Nierentuberkulose, *Beitr z klin d Tuberk* **71** 625, 1929.

18 Wildbolz Hans. Renal Tuberculosis, *J Urol* **21** 145 1929.

are alive and all but 3 have remained cured of the urogenital tuberculosis. Almost all of his patients who are alive more than ten years after nephrectomy have lost their vesical symptoms and urinate normally.

Merely finding the bacillus of tuberculosis in the urine is not sufficient evidence on which to make a diagnosis of renal tuberculosis. Its presence may be due to so-called tuberculous bacilluria. Bacilli of tuberculosis may pass through the kidney and appear in the urine without eliciting microscopic changes in tuberculous tissue, and without causing the admixture of pus in the secretion of the kidney. Wildbolz stated that the other microscopic observations are important, and above all the results of the functional tests should help to determine the diagnosis.

The healing of clinically demonstrable caseous renal tuberculosis if it occurs is extraordinarily rare. Nephrectomy in cases of bilateral renal tuberculosis is hardly ever justified. Removal of the kidney should be limited to cases of unilateral renal tuberculosis. Wildbolz expressed the belief that greater accuracy in diagnosing renal tuberculosis will eliminate futile and harmful procedures and that nephrectomy will bring permanent cure to many sufferers.

Medlar<sup>19</sup> expressed the belief that excretory bacilluria does not exist unless ulcerative tuberculous lesions are present in the kidney. There may not be any outward manifestations of renal tuberculosis. Infection is usually bilateral and hematogenous. He stated that some tuberculous lesions of the kidney do heal. Medlar agreed with Wildbolz as to the indications for nephrectomy and that if the lesion is bilateral removal of one kidney is contraindicated. Benign forms of renal tuberculosis of man are not of avian origin.

Papin<sup>20</sup> stated that there are three cardinal symptoms of renal tuberculosis, frequency (especially at night) pain during urination and pyuria. There are a few exceptions to this rule, which constitute clinical varieties of renal tuberculosis. He mentioned some of the main types. Pyuria in which there is false albuminuria, few vesical phenomena but slightly cloudy urine with albuminuria, the latter often misleading the diagnosis. Hematuria often appears in apparently normal persons and is frequently a sign of danger. In hydronephrosis with stricture of the ureter, complete obstruction may result. Tumor occurs especially in cases of excluded kidneys, such as hydronephrosis and closed pyonephrosis. Chronic nephritis of renal tuberculosis is rare and is the result of closed tuberculosis with sclerosis of the remaining portion of the organ.

19 Medlar, E. M. Discussion of Renal Tuberculosis. *J. Urol.* **21** 167 1929

20 Papin, E. Les variétés cliniques de la tuberculose rénale. *Paris. med.* **69** 328, 1928

Renal tuberculosis with incontinence rarely occurs, it is more common in children, when it occurs in an adult it is of great diagnostic value.

Dourmashkin<sup>21</sup> has observed that on the affected side in cases of renal tuberculosis the normal pelvic curve of the ureter is obliterated and the catheter goes up to the kidney in an almost straight line. As measured from the tip of the ischial spine, the distance from the catheter to the side of the pelvis is usually greater on the affected side than on the normal side. Dourmashkin concluded that the obliteration of the curve of the pelvis is probably due to a shortening of the ureter as a result of a tuberculous lesion. If the sign is present in conditions other than tuberculosis, ueteropyelographic study should be carried out. The condition has been observed in cases in which lesions are not apparent. Its frequent occurrence in patients with tuberculosis should render it of diagnostic value in doubtful cases or when the tuberculous infection is not suspected.

*Hyperplasia*—Pack and Buzzanca,<sup>22</sup> in a study of hydronephrosis and hyperplastic changes in the pelvic mucosa, introduced sterile pebbles into the renal pelvis of experimental animals. From these experiments they concluded that hyperplasia of the transitional epithelium of the renal pelvis is a frequent and early response to the presence of renal stones. Benign villous papillomas of the renal pelvis occasionally follow irritation by renal stones. This occurs later than the more common simple epithelial hyperplasia. Urinary stasis is suggested as one of the factors involved in the formation of tumor within the renal pelvis.

*Actinomycosis*—Cumming and Nelson<sup>23</sup> reviewed 9 cases of so-called primary actinomycosis of the kidney and added the data of two cases of their own.

The urinary tract is a relatively common site of actinomycosis, which should be considered a systemic, not a local, disease. The involvement of the kidney or ureter is usually secondary. When the process is apparently confined to the kidney, perinephric abscess is likely to occur. The disease is recognized by finding the typical granules in the urine, in pus from suppurating areas or in the tissues themselves.

The prognosis is usually grave, in secondary involvement the disease is so widespread as to be usually fatal, when primary in the kidney, it is well advanced when treatment is undertaken. Nephrectomy is the best treatment when applicable. Roentgen therapy, potassium iodide and

21 Dourmashkin, R. L. A Roentgen-Ray Sign in the Diagnosis of Unilateral Renal Tuberculosis, *J Urol* **21** 455, 1929.

22 Pack, G. T., and Buzzanca, Ross. Experimental Production of Epithelial Hyperplasia of the Renal Pelvis, *Am J Surg* **7** 221, 1929.

23 Cumming, R. E. and Nelson, R. J. Actinomycosis of the Urinary Tract, *Surg Gynec Obst* **49** 352, 1929.

copper sulphate are recommended but are only of accessory value after surgical drainage and removal of the affected organ

*Essential Hematuria*—Warsch<sup>24</sup> in further elaboration of eliminating cases from the so called essential hematuria class cited 3 cases in which the bleeding was explained by subepithelial hematomas in a chronically inflamed pelvic wall. Macroscopic and microscopic examination of the renal parenchyma failed to give any clues to account for the profuse bleeding. These cases illustrate the importance of examining the entire kidney carefully before classifying the case as one of essential hematuria

#### Ureter

*Tumor*—Thomson-Walker<sup>25</sup> reported 3 cases in which nephrectomy was performed for a papillomatous growth in the renal pelvis and in which at the time the ureter and bladder apparently were not involved. Papilloma of the ureter and bladder developed later, necessitating ureterectomy and treatment by electrocoagulation. Owing to the fact that ureterectomy was performed in these 3 cases within a period of six months one would be led to believe that papilloma of the renal pelvis was a condition increasing in frequency. In a large proportion of the recorded cases it was noted that the growth spread to the ureter and to the wall of the bladder at the corresponding orifice of the ureter. By performing nephrectomy the recurrence in ureter and bladder might possibly be prevented. It is evident that examination of the segment of ureter at the time of nephrectomy may be misleading, and that removal of the ureter should be carried out simultaneously with nephrectomy when the condition of the patient permits

[Compilers' Note—Recurrence of papilloma in the ureter and bladder frequently occurs. At cystoscopic examination the bladder may appear to be normal. Small papillomatous transplants may be found protruding from or surrounding the ureteral orifice. The papillomatous growths in the renal pelvis, as well as those in the ureter, are more compact than the transplants to the urinary bladder. Most tumors of the renal pelvis are malignant histologically. The transplants to the lower part of the urinary tract extension to the adjacent tissues and local recurrences make these tumors all clinically malignant. Because of the frequency with which the ureter is involved and the repeated recurrences after nephrectomy, complete nephro-ureterectomy is essential to insure even partial success.]

<sup>24</sup> Warsch, Ninon. Zur Frage der sogenannten "essentiellen Hämaturie" der Niere, *Ztschr f urol Chir* 26 339, 1929

<sup>25</sup> Thomson-Walker. John. Three Cases of Ureterectomy for Papilloma with Comments *Brit J Urol* 1 141, 1929

*Ureteral Transplantation*—Lisovskaja<sup>26</sup> noted that the mortality statistics of Russian surgeons in ureteral implantations to the rectum for benign lesions, such as fistulas and exstrophy, are about 31 per cent, those of the Mayo Clinic are 20 per cent. He is of the opinion that the latter low percentage in the Mayo Clinic is due to the two-stage operation employed there. In the Russian clinic the method is combined with a prepared autogenous vaccine of the colon bacillus. Two cases in which this method was used progressed satisfactorily. The interval between operations in one case was two months and in the other, six months. Lisovskaja also reported the cases of 3 patients who have remained well ten, twelve and fifteen years, respectively.

[Compilers' Note—Coffey's recent development of his technic of ureteral implantation based on clinical and experimental work done a number of years ago leads us to hope that this operation will become better standardized and thus be made available to the average urologic surgeon in a relatively short time. From the Mayo Clinic come interesting and encouraging reports of cases in which the patients are thus satisfactorily treated each year, with a definite lowering of the immediate and ultimate mortality. C. H. Mayo was one of the first to use this operation in exstrophy of the bladder. A number of years ago Kidd advocated total resection of the urinary bladder for inoperable neoplasm, the procedure being preceded by implantation of the ureter. The mortality of the operation at that time was prohibitive so far as general adoption of the method was concerned. If the mortality of ureteral implantation can be decreased to a relatively low degree, malignancy of the bladder and probably of the prostate gland can be more radically handled than our present surgical procedures permit. The perseverance of American surgeons, led by Coffey and C. H. Mayo, in overcoming apparently insurmountable technical difficulties and in developing this field of surgery is to be commended.]

*Stricture*—Frater and Braasch<sup>27</sup> concluded, from a study of the data from 93 necropsies, that the incidence of inflammatory stricture of the ureter is not so great as recent postmortem studies indicate and that diagnosis of stricture of the ureter by clinical methods now used may be inaccurate. The fact that the infectious origin of stricture of the ureter does occur is generally recognized, but no instance of this type of stricture was observed in their series. The greatest anatomic narrowing in the normal ureter usually occurs within the first 4 cm. from the

26 Lisovskaja, S. Auf welchem Wege ist die Mortalität bei der Ureteren-implantation in den Darm herabzusetzen? *Kuban nauchno-med* 7-8 40, 1928, abstr., *Ztschr. f. urol. Chir.* 26 189, 1929.

27 Frater, Kenneth and Braasch, W. F. The Incidence of Stricture of the Ureter, *Surg. Gynec. Obst.* 48 390, 1929.

ureteral orifice which corresponds to the area in which most strictures have been reported. Asymmetry in the two ureters was common; in several cases the caliber of one ureter was 50 per cent greater than that of the other, although both were normal on gross and microscopic examination. Ureteral dilatation, even when it occurs proximal to a portion of the ureter with a comparatively small lumen, does not necessarily indicate stricture. The dilatation in such cases may be atonic and the result of intrinsic chemical changes in the wall of the ureter. Stricture is not necessary to the formation of renal or ureteral stone.

*Ureteral Anastomosis*—Bump and Crowe<sup>28</sup> examined 6 dogs at varying periods after division and suture of the ureters. The urine had been excluded from the site of repair and the full caliber of the ureter had been maintained. Healing occurred without narrowing or appreciable dilatation of the lumina, with a minimal scar, without change in the renal pelvis and without evidence of severe injury to the kidneys.

Ten months after a similar repair of a ruptured ureter in a woman the ureter was found to be only slightly dilated, the renal pelvis and calices were not appreciably altered.

*Reflux*—Gruber<sup>29</sup> experimented with the intravesical portion of the ureter to determine whether there can be reflux of urine into the ureter from the bladder. He concluded that the intravesical portion serves as a true valve which acts passively and is not a sphincter dependent on muscle tonus or muscle contraction. In bladders of human beings, cats, dogs, pigs and monkeys, having normal valves, regurgitation does not occur, unless the injection pressures are excessive and the volume of fluid injected exceeds that normally found in the bladder. Cutting away the ureterovesical valve permitted reflux of fluid from the bladder into the ureter in all bladder tests, except in one human bladder with a thick wall. Stretching the mucosa of the bladder by injecting into the bladder excessively large amounts of fluid under high pressure shortens the valves and in many instances renders them incompetent.

[Compilers' Note—Gruber's composite study of the ureterovesical valve is interesting especially from the standpoint of comparative anatomy. The fact that the valve in the rabbit differs from that in other animals is important as the rabbit has been most extensively used in experimental work in this field. That the ureterovesical orifice does become incompetent at times in the face of urinary back-pressure such as is produced by obstruction of the vesical neck, is attested to by cystograms, which, as Bumpus and others have shown, frequently indicate reflux into the ureters. Such reflux is also noted at times in the cysto-

<sup>28</sup> Bump, W. S. and Crowe, S. M. Uretero-Ureteral Anastomosis. Surg. Gynec. Obst. **48**: 346, 1929.

<sup>29</sup> Gruber, C. M. The Uretero-Vesical Valve, J. Urol. **22**: 275, 1929.



gram in the presence of a tabetic bladder or when cystography is carried out under caudal or spinal anesthesia. The practice of ureteral meatotomy, which formerly enjoyed such a vogue, is today being more and more abandoned by many urologists on account of subsequent reflux of urine into the ureter and consequent renal infection. This is in accord with Gruber's experimental observations.]

#### BLADDER

*Tumor*—Hunt<sup>30</sup> reported that less than half of the patients with carcinoma of the bladder seen at the Mayo Clinic are amenable to the surgical procedures of excision of the lesion or segmental resection of the bladder.

The surgical excision of lesions affecting one or the other ureter has been difficult, owing to the necessity of properly disposing of the ureter. Extensive segmental resections have been done with consequent involvement of a ureter or ureteral orifice, and the ureter has been reimplanted into the bladder or ligated with a nonabsorbable ligature. A lower mortality has attended ligation of the ureter, nephrectomy on the affected side was required in only about 5 per cent of the cases. Ascending infection has been the cause of about 30 per cent of the immediate mortality when the ureter has been reimplanted into the bladder.

Surgical diathermy has been applicable in lesions of the base of the bladder which have been unsuitable for excision or segmental resection. It is doubtful whether surgical diathermy may be considered as superior to surgical methods in cases in which excision or segmental resection is possible. Hunt stated that a resectable lesion is more successfully treated by surgical excision.

Cystectomy is feasible in only a few instances. Usually when the lesion is unsuitable for excision, resection or surgical diathermy or other physical agents, cystectomy is out of the question because of extravascular extension, remote metastasis, partial or complete ureteral occlusion by the lesion, or the poor condition of the patient. In 1923, 63 cases of cystectomy were reviewed in which the mortality rate was 40 per cent.

Disposition of the ureters has been one of the difficulties of cystectomy. In some cases the operation has been facilitated by preliminary ureterostomy to the loin or inguinal area. In a number of reported cases in which the ureters were transplanted into the sigmoid or rectum simultaneously with cystectomy, there was a high mortality rate. The introduction of ureteral catheters into the ureters and taking them out through the cystectomy wound, or to the surface of the skin, simulta-

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30 Hunt, V. C. Transplantation of the Ureters into the Sigmoid, and Cystectomy for Carcinoma of the Bladder, Report of a Case, Proc. Staff Meet. Mayo Clin. 4: 233, 1929.

neous with cystectomy has been a dangerous procedure because of ascending infection of the kidneys. The high mortality rate in transplantation of the ureters simultaneously with cystectomy does not justify its use as a one-stage operation. In malignant conditions transplantation of ureters is accompanied by more risk than when it is necessary for such conditions as ectrophy of the bladder or irreparable vesicovaginal fistula. Simultaneous transplantation of both ureters is accompanied by greater risk than transplantation of one ureter at a time with a minimum of two weeks between operations.

When conditions justify cystectomy it may be done with less risk if the ureters are transplanted into the sigmoid one at a time, preliminary to cystectomy and if the bladder is removed several weeks later after good renal function and urinary control have been established with the ureters in the sigmoid thus confining the cystectomy entirely to an extraperitoneal operation.

Hames<sup>31</sup> stated that a simple uniform classification of tumors of the bladder is needed before any definite and satisfactory procedure of treatment can be attained. Each type of growth should be submitted to one plan of treatment and the results carefully tabulated.

Endovesical fulguration preceded by roentgen irradiation is the best treatment for papilloma and early papillary carcinoma when there is no evidence of infiltration and when intractable cystitis is not a complication. In doubtful cases this procedure is worthy of trial. In cases in which definite evidence of infiltration exists with the tumor favorably situated and not involving ureteral transplantation, and the patient is a good operative risk resection preceded by roentgen treatment is recommended.

For inoperable tumors roentgen irradiation followed by intensive diathermy and by cystotomy, may prolong life. Radium destroys the tumor in certain instances but it does not appreciably lengthen life, it has usually added to the morbidity and hastened death.

Roentgen treatment should be administered before any other treatment as it does not interfere with subsequent procedures, is harmless when properly applied, and is of some value in many instances.

Hermann,<sup>32</sup> in studying a series of 10 cases of carcinoma of the gastro-intestinal tract in the male noted that metastasis occurred in the urinary bladder in only 1 instance, whereas it occurred in 6 of 12 cases of Krukenberg's tumor. In these the bladder was involved simultaneously with the tubes and the uterus. The ovaries seem to be a

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31 Hames, W. H. The Treatment of Bladder Tumors, *Penn. M. J.* **32** 402, 1929.

32 Hermann, H. B. Metastatic Tumors of the Urinary Bladder Originating from the Carcinoma of the Gastro-Intestinal Tract, *J. Urol.* **22** 257, 1929.

determining factor in directing metastatic formation to the pelvic organs. When the ovarian tumor is accompanied by involvement of the pelvic organs operative treatment is not feasible. Symptoms referable to the bladder in cases of Krukenberg's tumor arise from the carcinomatous infiltration of the bladder.

Kaufman<sup>33</sup> stated that hematuria is the most significant sign of carcinoma of the bladder and requires cystoscopy if the patient is more than 50 years of age. The disease is local, has little if any tendency to metastasize but has unusual infiltrative qualities. The type of growth, the site and the structural changes should be ascertained before treatment is instituted. Radical operation, transperitoneal or extraperitoneal, offers the only possibility of cure in cases in which the growth is resectable, with transplantation or high ligation of the ureter when necessary. Radium treatment does not cure in frankly malignant tumors. With or without desiccation, it may be of value in treating small papillary tumors when employed through the cystoscope or by the suprapubic route. Roentgen irradiation is only a palliative measure for pain and occasionally for hemorrhage. Surgical diathermy is an excellent procedure in surgical resection of a tumor and is an efficient agent in checking the growth of the neoplasm in inoperable cases.

A significant symptom of carcinoma of the prostate gland is pain or urinary difficulty, and rectal examination is essential if patients are more than 50 years of age. Metastasis and extension in prostatic carcinoma overshadow the relatively small potential focus of malignancy. Radium is used effectively in limiting the return of the growth, and may be combined with a palliative operation for the relief from urinary obstruction. Permanent suprapubic cystotomy, combined with radium, gives the best general outlook. Radical prostatectomy is limited to only a small group of cases of carcinoma of the prostate gland.

[Compilers' Note—It would appear that in no field of urologic thought is there so much controversy as that concerning vesical neoplasms. Operation, radium, roentgen rays, diathermy and fulguration have their proponents. During the last few years total cystectomy with ureteral transplantation into the large bowel found an increasing number of advocates. Most urologists are agreed that smaller papillomas should be treated by fulguration. As for the value and possible danger of biopsy, there is dispute but most men favor it. Partial cystectomy when practical and possible of being carried out with reasonable technical ease is still widely practiced, but many surgeons urge that this is done only if tumors are well localized and of a relatively low degree of malignancy. Diathermy or electrocoagulation through an open cystotomy wound for

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<sup>33</sup> Kaufman, I. R. Tumors of the Bladder and Prostate with Special Reference to Cancer. *S. Clin. N. Amer.* 9:701, 1929.

tumors of higher malignancy may be used hopefully. This however is not without danger as some instances of marked sloughing are reported. Ureteral implantation into the bowel as is being carried out by Coffey and at the Mayo Clinic with an ever decreasing mortality leads us to hope that eventually this procedure followed by total cystectomy will be the solution of the problem of dealing with extensive tumors of the bladder.

Kauffman voices the general opinion in regard to carcinoma of the prostate gland. The advocates of radical prostatectomy are far in the minority but a few surgeons such as Young and Wildbolz report enough success in early cases to make a consideration of the procedure reasonable and worthy of trial in isolated instances in which the operator discovers malignancy in a gland that has preoperatively been diagnosed as benign.]

Harrison<sup>34</sup> in reviewing 178 cases of carcinoma of the bladder concluded that the best results are obtained in selected cases, from radical operation with resection of the bladder and transplantation of the ureter. When resection was inadvisable and the case was not too advanced or complicated with metastasis a combination of cystotomy, diathermy and roentgen irradiation resulted in improvement of the condition in 70 per cent of the cases and of amelioration of symptoms in 90 per cent for varying lengths of time.

Harrison also reviewed 48 cases of carcinoma of the prostate gland. Operation is the procedure of choice if the diagnosis of carcinoma of the gland can be made while it is still confined within the capsule. Radium implants used in conjunction with roentgen rays prolonged life and improved symptoms in more than 70 per cent of the cases.

Brvan<sup>35</sup> reported a case of sarcoma of the bladder. He noted that sarcoma comprises 56.9 per cent of all infantile tumors of the bladder. Sarcoma of the bladder may result as an extension of growth from the surrounding structures and may be of the round cell or spindle cell variety, pedunculated, sessile or infiltrating. It is extremely malignant as evidenced by metastasis, cellular changes, irregularity in size and shape and staining of the nuclei, abundant nuclei and mitosis. The growths are most often situated about the trigone but if they are on the wall of the bladder, they bulge or hang like a cluster of grapes.

There are two types of sarcoma, the polypoid tumors, which hang bunchlike, are of rounded elevations of mucous membrane with a more or less constricted base, and the infiltrating, general round cell or spindle

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34 Harrison, F. G. End Results of Carcinoma of Bladder and Prostate Gland, Penn. M. J. **32**: 407, 1929.

35 Brvan, R. C. Sarcoma of the Bladder. Report on a Case. J. Urol. **21**: 695, 1929.

cell sarcoma involving essentially the connective tissue planes of the bladder with wide and symmetric dissemination. Occasionally sarcomas may be pedunculated, but they are usually sessile, with broad bases. Metastasis is common in the retroperitoneal lymph nodes and in the structures about the bladder. Metastasis occurs only by the blood stream and by direct continuity.

The earliest and most reliable symptom is hematuria, which occurs in 62 per cent. The amount of hemorrhage apparently is not indicative of the extent of the tumor.

Bryan referred to Munves' report of 69 cases of sarcoma of the bladder, 38 patients died soon after operation, and only 3 were considered cured.

*Leukoplakia*—Bugbee<sup>36</sup> reported a case of leukoplakia in a diverticulum of the bladder. The diverticulum, lying to the right of the bladder and posterior to it, was resected. The vesical orifice was thoroughly dilated. The mucous membrane of the bladder was normal except for moderate congestion. Pathologic examination revealed leukoplakia-like areas in the denser portion of the diverticulum.

Leukoplakia is almost always associated with long-continued, chronic infection, it progresses slowly, and the only cure is by excision. It is apparently a necessary preliminary to epidermoid or squamous cell carcinoma. Bugbee stated that the possibility of its occurrence in a diverticulum of the bladder is a strong argument for the early removal of a diverticulum by resection.

*Eisnophy*—Turner<sup>37</sup> reported 17 cases of transplantation of ureters into the bowel for congenital defects, with 4 deaths (23.5 per cent) directly due to the operation. One patient died more than three years after operation and another more than two years, both having been in good health during the interim. Of the remaining 11 patients, 1 is included twice, which leaves 10 patients alive and well at periods varying from fifteen years to seven months after operation. In most cases the operation was performed in two stages, a total of twenty-eight separate operations, making the mortality 14.3 per cent. Considering that there were twenty-nine separate transplantations of the ureters, with four deaths, the mortality is 13.8 per cent. In a series of 60 cases in the Mayo Clinic the mortality was 13.33 per cent. The cause of death in 3 of Turner's cases was peritonitis. The fourth death occurred in a child aged 1 year and 4 months from general septic dermatitis.

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<sup>36</sup> Bugbee, H. G. Leukoplakia in a Diverticulum of the Bladder, *J. Urol.* **21** 395, 1929.

<sup>37</sup> Turner, G. G. The Treatment of Congenital Defects of the Bladder and Urethra by Implantation of the Ureters into the Bowel, with a Record of Seventeen Personal Cases, *Brit. J. Surg.* **17** 114, 1929.

Fatalities usually have occurred either when both ureters were transplanted at one time, or after the transplantation of the second ureter in the divided operation. In general, Turner's operative technic is similar to that employed by C. H. Mayo and by Coffey.

The general health of the 10 surviving patients was found to be practically normal. It sometimes takes months or even as long as two years before patients become accustomed to the altered state. Meanwhile, they are acquiring complete rectal toleration, and the kidneys are presumably accommodating themselves to the element of constant mild infection. The time required for the lower part of the bowel to become accustomed to the presence of urine and to the unusual amount of fluid is variable. The younger the patient, the less the control at first. After the second stage of the operation, toleration at night comes rather quickly. Immediately after the operation and for the first day or two, the urine seems to flow constantly from the anus. Owing to the fact that the presence of a foreign body in the anus is greatly resented, Turner does not always persist in keeping a catheter in the bowel. Once toleration has been acquired, most patients can retain urine for several hours during the day, and nearly all night, without discomfort. The average length of time was ascertained to be three hours, the longest period was four and a half hours. Most of the patients get up once at night, sometimes two or three times.

None of the patients of this series showed definite evidence of gross renal insufficiency. That some degree of ascending renal infection develops is borne out by the fact that in two postmortem investigations there was definite, gross evidence of its existence, although neither patient suffered from symptoms indicating its presence. Among the 10 living patients there are 3 who at seven years, three years and three months, and eight months after operation had not suffered from symptoms of renal infection. A moderate degree of renal infection apparently is not inconsistent with average good health. Turner's patients are in good average health and able to withstand the trials of their ordinary environment. Several of them successfully underwent operations under general anesthesia without unusual symptoms. One patient was not more than ordinarily disturbed by pregnancy and lactation. The fact that both patients who died after operations subsequent to the transplantations showed acute renal infection added to the gross and long-standing changes, is not in his opinion evidence that they were suffering in that way before their fatal illness.

*Rupture*—Sisk and Wear<sup>38</sup> reported a case of spontaneous rupture of the urinary bladder of the extraperitoneal type. There are two types

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<sup>38</sup> Sisk, I. R. and Wear, I. B. Spontaneous Rupture of the Urinary Bladder, *J. Urol.* 21: 517, 1929.

of spontaneous rupture of the bladder, the extraperitoneal and the intraperitoneal, depending on the site of the perforation. Extraperitoneal rupture is less common and less grave than the intraperitoneal type.

The etiology of spontaneous rupture of the bladder depends on some obstruction to urination or interference with the nerve supply of the bladder, resulting in distention of the bladder. The secondary factor is usually pathologic change in the wall of the bladder.

Symptoms and diagnosis depend on whether the rupture is intraperitoneal or extraperitoneal. In either type, the history of previous urinary difficulty and the finding of some type of obstruction is significant. In the extraperitoneal cases there is pain and swelling above the pubis, which soon results in the formation of pus. Because of the seriousness of the intraperitoneal type, early diagnosis is important. At the time of rupture, the patient usually experiences sharp abdominal pain and some shock. Normally there is marked desire and difficulty of urination.

The treatment in both types of spontaneous rupture of the bladder is immediate operation. In extraperitoneal rupture, if the condition of the patient permits, good results are obtained by the introduction of a suprapubic tube and relief from the direct cause. In the intraperitoneal type the abdomen should be opened and drained, and the opening in the bladder closed in layers, with adequate drainage provided by an indwelling urethral catheter or a suprapubic tube.

*(To be concluded)*

# ARCHIVES OF SURGERY

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## THE RECOGNITION OF ELEPHANTIASIS AND OF ELEPHANTOID CONDITIONS BY SOFT TISSUE ROENTGENOGRAMS

WITH A REPORT ON THE PROBLEM OF EXPERIMENTAL LYMPHEDEMA \*

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SAN FRANCISCO

Although elephantiasis has been described for centuries the involvement of the lymphatics in this disease was not recognized until the extent of the lymph channels in the body had been revealed by the work of many anatomists and until physicians in the tropics had found filarial organisms blocking the lymph vessels and lymph nodes

### THE LYMPHATIC SYSTEM

The universality of this system throughout the body was vaguely recognized in the eighteenth and nineteenth centuries. Until recently, knowledge of the lymphatic system was limited to anatomic studies of these thin walled valvular vessels in various parts of the body as demonstrated by the injection method. It was known also that there were two sets of lymphatics in the extremities a superficial and a deep group which eventually drained into deeply situated lymph nodes. This is well illustrated in an old chart (fig 1)

Of the many anatomists who have studied the lymphatics, one feels that if William Hunter had lived a little longer, he and his pupil Cruickshank would have contributed an earlier understanding of the importance of this system in its relation to the vascular system and in its economy in body function. By Hunter's death the work was left to Cruickshank, who, hampered by lack of funds, was able to prepare only a few sketches to illustrate his monograph on the lymphatic system. In the William Hunter Museum in Glasgow the many beautiful specimens of lymphatics filled with mercury stand today as ready to be carefully described and correlated as when they were prepared over a hundred years ago

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It remained for others in this country to repeat the injections made by these Glasgow anatomists. The first approach by modern investigators was made by studies of embryonic injections. Just as the origin of the arterial and venous systems had been revealed by embryonic studies, so the investigations of a number of workers, notably Sabin

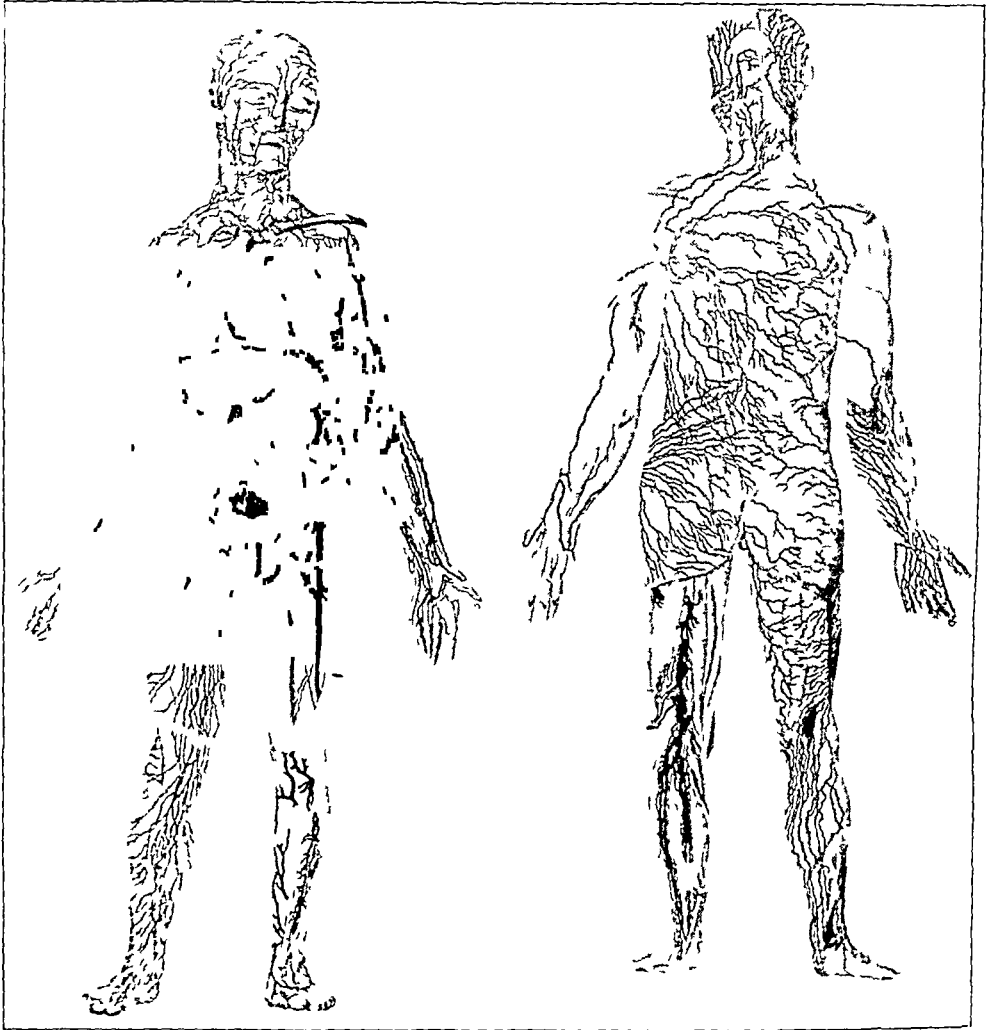


Fig 1—Old chart of the lymphatic system, showing the superficial and deep sets of lymphatics in the extremities which eventually drain into deeply situated lymph nodes

and her pupils, present a fairly complete picture of the origin of the lymphatic system and its correlation with the lymphatics in the adult. It is known that as modified veins, lymphatics have a specific function in absorption although the complete physiology of this system is not as yet established.

The present teaching concerning lymphatics makes them a system as objective and definite as that of the arteries and veins. Just as there are definite blood capillaries, so there are definite lymphatic capillaries and tissue spaces. Sabin<sup>1</sup> suggested that if the name "plasma" is reserved for fluid within the blood vessels, "lymph" for the fluid within the lymphatics and "tissue fluid" for the fluids of the tissue spaces conceptions would be greatly clarified. Just as blood capillaries grow through proliferation of their own walls and regenerate when divided, so do the lymphatic capillaries regenerate a little more slowly than the veins. Infection and scar tissue interfere with the growth of blood capillaries and likewise hinder the regeneration of lymphatic capillaries.

The importance of the lymphatic system in the maintenance of circulatory balance has been emphasized by Halsted<sup>2</sup> and I have shown it experimentally.<sup>3</sup> A limb in its normal state requires a balance of the efferent vessels of the arterial system with the afferent vessels of the lymphaticovenous system. A disturbance on the afferent side may lead to edema as a result of venous or capillary derangement or it may be caused by lymph stasis. Frequently this edema is due to disturbances of the interdependent lymphatic and venous systems.

#### THE EDEMAs

True lymph edema caused by division or blockage of lymph channels, usually involves both the dermal and the subcutaneous structures but not the deeper tissues. It produces a brawny, leathery condition of the integument, and the dermal distention often gives an "orange peel" appearance to the surface of the skin. There is no definite pitting on pressure of the skin. It occurs after bilateral glandular dissection of the neck particularly on the facial side of the incision and is not evident until the second postoperative day. It usually subsides completely within a week or ten days but may persist for two weeks or longer if the regeneration of lymphatics across the wound has been delayed by poorly approximated tissues or by infection. Lymphedema is sometimes seen in carcinomatous breasts, and it may produce the enlargement found in Milroy's disease, although in two of the three cases of this disease which I have seen, infection had been superimposed on this condition. Clark and Clark<sup>4</sup> experimentally produced generalized lymphedema by removal of the lymph hearts in embryos.

1 Sabin, F. R. The Growth of the Lymphatic System, The Harvey Lectures, 1915-1916, Philadelphia, J. B. Lippincott Company, p. 124.

2 Halsted, W. S. Replantation of Entire Limbs Without Suture of Vessels, *Proc. Nat. Acad. Sc.* 8: 185, 1922.

3 Reichert, F. L. The Regeneration of the Lymphatics, *Arch. Surg.* 13: 871 (Dec.) 1926.

4 Clark, E. W. and Clark, E. R. The Character of the Lymphatics in Experimental Edema, *Anat. Rec.* 21: 127 (May) 1921.

Vascular edema, pitting edema or "dropsy," presents a different picture. This edema exists throughout all the structures, especially in the subcutaneous tissue and muscle, and does not particularly involve the dermis. The skin is tense and smooth and pits readily on pressure. The edema is usually more marked in the lower extremities or limited to them, although it may be generalized. It diminishes readily when the part is elevated. It is generally the result of capillary damage and stasis in cardiovascular or renal disease and can be produced by division or blockage of all the veins to a part.

Neither lymphedema nor vascular edema, even of long duration, will lead to a proliferative change and deposition of fibrous connective tissue. When, however, infection or toxemia is superimposed on a derangement of the lymphaticovenous system, a condition of elephantiasis may develop.

#### ELEPHANTIASIS

Matas<sup>5</sup> gave a comprehensive definition and description of this condition.

By elephantiasis we mean a progressive histo-pathologic state or condition which is characterized by a chronic inflammatory fibromatosis or hypertrophy of the hypodermal and dermal connective tissue which is preceded by and associated with lymphatic and venous stasis, and may be caused by any obstruction or mechanical interference with the return flow of the lymphatic and venous currents in the affected parts. In order to bring about the hypertrophy of the connective tissue, which is the distinct feature of the true elephantiasis state, the mechanical impediment to the lymphatic and venous drainage of the part is not sufficient, because a simple mechanical obstacle, while causing a regional or localized dropsy or lymphedema, will not bring about the characteristic fibromatosis and other histologic changes which are peculiar to elephantiasis. As Unna, Darier and many others have well shown, a simple mechanical edema is incapable of exciting a proliferation of the collagenous connective tissue. We know by clinical observation that edema may exist many years in the extremities and other parts without causing any fibromatosis or hyperplasia of the connective tissue of the parts. Something more than lymph stasis is required, and that something is infection with pathogenic organisms, and especially those of the streptococcal type which find a favorable soil for development in the stagnant lymph stream. The histopathological elements which are essential to complete the picture of elephantiasis are (1) a mechanical obstruction or blockade of the veins and lymphatics of the region, usually an obliterative thrombo-phlebitis or lymphangitis or adenitis, (2) hyperplasia of the collagenous connective tissue of the hypoderm, (3) gradual disappearance of the elastic fibers of the skin, (4) the existence of a coagulable dropsy or hard lymphedema, and (5) a chronic reticular lymphangitis caused by secondary and repeated invasion of pathogenic microorganisms of the streptococcal type.

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<sup>5</sup> Matas, R. The Surgical Treatment of Elephantiasis and Elephantoid States Dependent upon Chronic Obstruction of the Lymphatic and Venous Channels, *Am J Trop Dis & Prev Med* 1:60 (July) 1913.

We have now come to realize that whatever the cause of the lymphedema may be, the element of infection is the one essential and determining factor in the production of true elephantiasis. In fact, if we accept the views of many writers such as Le Dantec, Sabouraud and Unna, the progressive fibromatosis which we recognize as elephantiasis nostras, may occur independently of any stagnatory state of the lymphatic or venous circulation, and solely as a result of repeated attacks of a streptococcal infection, which has been regarded by many as identical with the erysipelas coccus of Fehleisen. Moreover, the streptococcal infection of elephantiasis presents all the characteristics of the classical cutaneous erysipelas with the exception that in elephantiasis it is usually limited to one particular region in the lower extremity, the eruption rarely extending beyond the groin.

That it is in the highest degree probable that the true sporadic cases of elephantiasis develop from incompletely healed erysipelas—that is, those which leave behind disturbances in the circulation. The streptococci remain latent in the tissues and in this way excite the chronic proliferative tissue changes which we subsequently recognize as elephantiasis. At first the attacks of erysipelas occur at long intervals, perhaps twice or three times a year, then once a month, rarely oftener. Each time the limb grows larger until in the course of time a distinct elephantiasic state is established. Natural immunity does not appear to be easily acquired, and once the erysipelatosus habit, so-called, is acquired, it usually becomes a permanent feature of the disease, though in some cases the attacks become milder and disappear altogether, but not until the elephantiasic state is fully established.

Halsted,<sup>6</sup> in considering the swelling of the arm after the radical operation for cancer of the breast, showed "that excision of the axillary and supraclavicular glands plus resection of the subclavian and axillary veins is rarely followed by noticeable swelling of the arm. On the other hand we do not deny that obstruction of these lymphatic and venous channels might conceivably alone, without infection, suffice occasionally to produce a moderate amount of oedema." His records tend to show that in all cases in which the swelling in the arm persisted, infection had been the main factor in its production and he termed this chronic indurated enlargement, elephantiasis chirurgica. As he pointed out many of the patients gave an account "of recurrent attacks of redness and increased swelling accompanied by digestive and constitutional disturbances. These attacks not infrequently ushered in by chills and fever" occurred at infrequent intervals from months to years apart.

This reaction, which accompanies the appearance of the local erysipelatosus rash, is what Sir Joseph Farrer termed elephantiasic fever. As Matas stated

The fever usually lasts from two to eight days and defervesces with the subsidence of the erysipelas which rarely extends beyond the root of the limb. During the attack, the skin of the affected region becomes red, painful, swollen and looks exactly like the erysipelas rash; the lymph nodes are enlarged and the red-

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<sup>6</sup> Halsted W. S. The Swelling of the Arm After Operations for Cancer of the Breast—Elephantiasis Chirurgica—Its Cause and Prevention, Bull. Johns Hopkins Hosp. 32:309 (Oct.) 1921.

ness diffuses itself with great rapidity over the entire surface of the limb. After the subsidence of the attack, the skin remains swollen, giving the impression of a soft, doughy oedema. The soft consistency gives place to a more permanent hardness, the skin of the affected part never returning to normal. The underlying soft parts unite with the skin, which increases very much in thickness, forming a firm, immovable mass of tissue which continues to grow until it finally assumes a monstrous size which is characteristic of the disease.

Beitwistle and Gregg<sup>7</sup> agreed that elephantiasis develops only "in cases of solid oedema after attacks of fever and lymphangitis." Considering the pathology of the disease, they stated

It appears necessary, therefore, that not only must there be a transudate of lymph, but that it must be changed in some way, as happens when it becomes an exudate as the result of inflammation. It has been shown that the lymph exudate in cases of elephantiasis is charged with albumin, and, as protein is a stimulant to cell activity and growth the key to the hypertrophy and hyperplasia probably lies in Starling's description of the function of lymph. "The only way the tissues can receive their supply of protein is from the small amounts which are filtered through the blood vessels into the lymph. The increased exudation of concentrated lymph which occurs in inflammatory conditions as the result of injury is therefore of advantage, since it furnishes an abundant supply of protein food to be used up in the regeneration of the damaged cells." In elephantiasis the affected part receives an increased supply of protein as the result of recurring attacks of inflammation, and it is suggested that this protein, instead of merely helping in the process of repair, serves by its continuous or prevented action to stimulate the connective tissues to excessive growth.

Some writers think that the toxemia produced by the death of the filarial organisms, rather than the infection, is the factor in causing elephantiasis tropicum. Beitwistle and Gregg mentioned a case reported by Manson-Buhr in which elephantiasis followed the toxic absorption of chrysarobin in the treatment for psoriasis. I have the records of two cases in which excision of the axillary lymph nodes was done, and in which incipient elephantiasis was present due to repeated attacks of malaise, fever and vomiting associated with pain and swelling of the affected extremity following the eating of shellfish. The excision was done in one case for carcinoma of the breast, and in the other for epithelioma of the hand.

#### EXPERIMENTAL WORK ON ELEPHANTIASIS<sup>8</sup>

According to Unna,<sup>9</sup> it would seem that Bockhart, Sabourand, Le Dantec and others have tested the development of elephantiasis in man

<sup>7</sup> Beitwistle, A. P., and Gregg, A. L. Elephantiasis, *Brit J Surg* **16** 267 (Oct.) 1928.

<sup>8</sup> The earlier portions of this investigation were carried on in the Hunterian Laboratory of Experimental Surgery, Johns Hopkins Medical School, with the assistance of Dr. Mont Reid and Dr. C. Y. Bidgood in 1920.

<sup>9</sup> Unna, P. G. *The Histopathology of Discases of the Skin* (Translated by N. Walker), New York, The Macmillan Company, 1896, p. 493.

by inoculation of pure erysipelas cultures, but so far as I know experimental elephantiasis has never been produced in animals

Attempts to produce elephantiasis in experimental animals were initiated by Professor Halsted in conjunction with his study on elephantiasis chirurgica following radical mammary amputations. The posterior extremities of cats and dogs were chosen as the most satisfactory operative area, and we first tried to produce edema by complete excision of the iliac and inguinal lymph nodes without success. Nor did it occur following ligation of the iliac or the femoral vein with excision of the regional lymph glands. We then attempted blocking the lymphatics by injections of gelatin, agar, paraffin, celloidin, bismuth and india ink into the lymphatic channels and lymph nodes. Only a slight transient swelling followed these methods of injection.

Finally, Professor Halsted suggested a transverse division of the thigh as a means of severing all lymphatics. The first experiment was made by Dr. Mont Reid and as he feared possible gangrene only a hemicircular division of the thigh was done. Again only a very slight edema appeared, and as neither gangrene nor infection developed, the rest of the limb was severed ten days later, leaving only the femur, femoral artery and vein intact. A definite swelling occurred distal to the incision and persisted for several days and for the first time a marked lymphaticovenous edema had been secured.

With improved technic a complete severance of the thigh by circular incision was performed at one operation, leaving in continuity only the carefully denuded femoral artery and vein and the femur stripped of periosteum (fig. 2 in my previous work<sup>3</sup>). All bleeding points in the muscle were tied off with fine silk and the limb was replanted by careful approximation of the aponeurosis of each muscle with interrupted fine silk sutures. The subcutaneous tissue and skin were likewise approximated with interrupted silk sutures. As a result of the most rigid aseptic technic and gentle handling of the tissues, these replantations healed per primam and with a minimum of scar formation, in the great majority of the experiments.

Invariably edema appeared in the replanted limbs on the second postoperative day, reached a maximum on the fourth or beginning of the fifth day and had subsided completely by the seventh or eighth day (fig. 2). By the use of Hill's<sup>10</sup> opaque roentgenographic mass injected into the arterial system, new arterial anastomoses were demonstrated at the end of the second day and were numerous on the third postoperative day. When a warm gelatin mass of lead chromate was injected through the arteries and capillaries into the venous system of the limb, new

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10 Hill, E. C. Notes on Opaque X-ray Mass. Bull. Johns Hopkins Hosp. 35: 218 (July) 1924.

venous anastomoses across the replanted area were evident at the end of the fourth and the beginning of the fifth day just when the swelling, as indicated by measurements, had reached a maximum or was beginning to subside. Further proof of venous regeneration was shown by the fact that for the first time since replantation, ligation of the only patent venous channel, the femoral vein, could be attempted without the development of gangrene. This procedure did not cause further edema, in fact, there was a delay of only one or two days in the subsidence of the swelling.

A previous report<sup>3</sup> offers these replantation experiments as a comparatively easy method for investigating the regeneration of both the superficial and the deep sets of lymphatics under what may be consid-



Fig 2—Photograph of a replanted limb when the lymphaticovenous edema was about maximum

ered normal conditions. The earliest lymphatic regeneration was shown to be four days after operation, at which time the new venous channels were also being formed. These new lymphatics were demonstrated in the superficial group, and by the eighth day, when the edema had completely subsided, regeneration was physiologically adequate in both the deep and the superficial sets of lymphatics. At this time ligation of the femoral vein caused no recurrence of the edema, but swelling reappeared when the lymphatics were blocked with granules of india ink. Evidently, then, the lymphatic system by its regeneration was of importance in producing a subsidence of the edema, and with the veins formed a lymphaticovenous system, the function of which lay in disposing of the edema and in reestablishing the circulatory balance. The experimental results of a study of the circulatory balance in these replanted limbs will be presented in another paper.

Delay in the subsidence of the swelling was secured in some cases at the time of operation, when long silk ligatures were loosely placed about the femoral artery and vein to facilitate the location of these vessels at a later date. The edema persisted for two weeks or more in these limbs, although there was no infection. In the region of the vessels, the silk had caused an inflammatory reaction which, as shown by injections of india ink, had interfered with the regeneration of the deep set of lymphatics.

In other experiments, attempts were made to delay the regeneration of the superficial set of lymphatics by the formation of considerable scar tissue in the skin and subcutaneous layer. The irritants used to produce the cicatrix were the actual cautery, or chemicals, such as carbolic acid and alcohol, iodine and indelible ink. When no infection occurred, edema remained for ten days or more and injections of india ink showed that a number of superficial lymphatics were blocked at the line of incision.

When the regeneration of both the superficial and the deep sets of lymphatics was interfered with there was a delay of from two to three weeks in the subsidence of the edema. In all these experiments, and in those in which infection of the wound occurred, the edema disappeared completely.

By such experiments we felt that a lymph and venous edema had been produced. Examination of the replanted limb at the fourth or fifth postoperative day demonstrated the edema existing throughout all the tissues. In the late stages of a delayed edema, such as that produced by interference with the regeneration of the lymphatics, the edema was mainly confined to the skin and subcutaneous tissues, being more nearly a pure lymphedema.

Infection superimposed on such an edema seemed the next step in the production of an experimental elephantiasis. It was hoped that repeated streptococcal inoculations would lead to the enlargement and fibromatosis of elephantiasis, but during the past eight years we have failed in its production although we have tried many methods of inoculation and have sought the advice of a number of bacteriologists. Dogs seem to be exceedingly resistant to streptococcal infections, the inoculations producing abscesses rather than lymphangitis. Occasionally veterinarians have had cases of canine lymphangitis, but either cultures were not taken or we were not able to secure live organisms. Our inoculations were made with streptococci obtained from patients with scarlet fever and erysipelas grown in twenty-four hour broth culture and then centrifugated to concentrate the bacteria. Injections were made both intradermally and subcutaneously in many replanted limbs at a time when the edema was subsiding or just after its disappearance. In only



one instance did an animal develop a lymphangitis, which spread over the white skin of the fox terrier like an erythematous rash and was followed by desquamation. Repeated inoculations brought no repetition of this canine scarlet fever.

Other methods, such as injections of the bacteria into the femoral artery and the distal veins of the replanted limbs and inoculations into excoriated skin areas, failed to initiate any evidence of lymphangitis.

The next step would seem to be the repetition of replantation experiments in an animal species more subject to lymphangitis.

#### THE ELEPHANTOID CONDITION

Elephantoid conditions are frequently seen and have been recognized by Matas<sup>5</sup> as follows:

But the majority of cases that come under our observation are elephantoid states, swollen limbs, and genitals, following chronic lymph oedemas of the dependent parts in which venous and lymphatic obstruction plays the leading role in the pathogeny. The starting point of these obstructions may be traced to injuries involving the circumference of the limbs at their root, or tumors blocking the deep lymphatics, chronic circular ulcers of the leg, syphilitic, tuberculous and phagedenic in origin, chronic phlebitis associated with varices, post typhoid, puerperal, chronic eczema and kindred conditions. In the upper extremity the arm and the hand are often seen swollen and brawny, with chronic lymph oedema in women who have neglected cancer of the breast and whose axillary vessels have been compressed by cicatricial contraction or by secondary neoplastic metastasis. These elephantoid states constitute an extremely unsightly, painful and disabling deformity which in the lower extremities especially, restrict the patient to a sedentary life.

Emphasis has again been placed by Homans,<sup>11</sup> Traut<sup>12</sup> and myself<sup>13</sup> on the common failure to recognize these frequent elephantoid conditions. Homans expressed the belief that a disturbance of the lymphatics underlies the process in thrombophlebitis of the deep veins of the legs (phlegmasia alba dolens). The milk leg is not cyanotic, as one would expect if only a great extent of vein were thrombosed. He attributed the white swelling to the inflammatory process associated with the thrombosis which promptly involves the accompanying principal lymphatic trunks which drain the limb, thus producing a lymph stasis of the entire extremity. Experimentally, he produced "milk leg" of ten days'

11 Homans, J. Thrombophlebitis of the Lower Extremities, *Ann Surg* 87 641 (May) 1928.

12 Traut, H. H. Ulcers Due to Varicose Veins and Lymphatic Blockage, A New Principle in Treatment, *Arch Surg* 18 2281 (June) 1929.

13 Reichert, F. L. Circulatory Disturbances of the Extremities with Special Reference to Thromboangitis Obliterans and Elephantoid Conditions, *California & West Med* 31 233 (Oct) 1929.

duration in a dog by introducing 2 cc of muscle juice into the lumen of an isolated segment of femoral vein. The resulting inflamed segment and perivenitis presumably blocked the adjacent lymphatic trunks, although this was not demonstrated by injection of these lymphatic vessels.

Working with Zollinger, Homans<sup>14</sup> extended his experiments and secured a transient lymph stasis due to demonstrable lymphatic blockage.

In 1926, I attempted to produce "milk leg" experimentally by inducing venous thrombosis. Only a slight transient swelling of the thigh developed after the injection of nonhemolytic streptococci or *Staphylococcus aureus* into isolated segments of the iliac vein. A moderate edema of the thigh, leg and foot of from four to seven days' duration followed intravenous injections of 20 per cent saline solution. In some instances venous thrombosis and perivenitis developed. The salt solution was kept within the vein for twenty minutes either by a tourniquet at the level of the groin or by the isolation of a portion of the external iliac vein between clamps. Cauterization of the vein with ensuing thrombosis and perivenitis was obtained by introducing a silver wire from a diathermy machine into the lumen of the saphenous and femoral veins. This resulted in an edema of the whole limb which lasted for eighteen days. Four days after cauterization a small hematoma appeared deep in the thigh which may have been a factor in the production of the perivenitis although there was no increase in the edema.

As Homans stated, the complication that occurs after phlegmasia alba dolens is usually "a porky oedema in the superficial tissues of the calf. This oedema sooner or later becomes indurated, the skin over it pigmented, and if the patient must spend much time in standing, the indurated area finally breaks down wholly or in part and becomes an obstinate ulcer." His postphlebitic indurations are really localized elephantoid areas.

Traut emphasized the importance of lymphatic blockage in the production of ulcers due to varicose veins. Both he and Homans advocated the removal of this elephantoid tissue, including the underlying muscular aponeurosis.

I agree with Matas that the chronically enlarged indurated legs, often with resistant ulcers, the background of which is the story of phlegmasia alba dolens, of long-standing varicose veins or of chronic infective processes of a pyogenic, syphilitic, tuberculous or fungoid nature, are in truth evidence of an elephantoid condition, differing from elephantiasis only in their extent and ulceration. The same chronic, inflammatory fibromatosis exists in true elephantiasis and one generally secures a history of infection or a story of repeated attacks of erysipelas.

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<sup>14</sup> Homans, I. and Zollinger, R. Experimental Thrombophlebitis and Lymphatic Obstruction of the Lower Limb. Arch Surg 18:992 (April) 1929.

## SOFT TISSUE ROENTGENOGRAMS

When Professor Halsted was so interested in elephantiasis, a few roentgenograms were taken of the involved limbs, which showed a great thickening of the superficial tissues. Since then all of our cases of an elephantoid nature, as well as some cases of edema due to cardiovascular or renal disease, have been roentgenographed to outline the tissues, and the films have been carefully studied. I<sup>13</sup> think that roentgenograms taken to define the soft tissues rather than bone offer a means of clearly differentiating the edema of an elephantoid nature from other types of edema. Roentgenograms of simple lymphedema show an enlargement of the tissues from the skin to the muscular layer, whereas the films of ordinary dropsy or vascular edema show a diffuse density or thickening which involves all of the tissues of the extremity.

In contrast with simple lymphedema, elephantiasis and elephantoid states present an entirely different picture in soft tissue roentgenograms. Not only do they show a great thickening of the dermis and marked enlargement of the subcutaneous tissues down to muscle with a thickened muscular aponeurosis, but the unique feature in this condition is an extensive network of fibrous trabeculations in the hypodermal layer. This roentgenographic reticulation is produced by the marked fibromatosis of the subcutaneous layer. Only in case of elephantiasis or elephantoid conditions do the roentgenograms reveal these trabeculations. These characteristic trabeculations were also found in the roentgenograms of a youth seen on the pediatric service with a familial history of bilateral congenital "lymphedema." No history of attacks of elephantiasis fever or infection of the leg was obtained, and the patient was considered as having an uncomplicated case of Milroy's disease.

## REPORT OF CASES

A few selected cases, with their soft tissue roentgenograms, will serve to illustrate simple edema, elephantiasis and elephantoid states.

CASE 1—G. O., a man, aged 50, for years had suffered from glomerulonephritis and for the past five months had had a continuous pitting edema. Soft tissue roentgenograms revealed a diffuse homogeneous cloudiness throughout the swollen leg. The roentgen appearance (fig. 3) was typical of that seen in edemas due to cardiovascular or renal disease.

CASE 2—In M. N., a woman, aged 71, a carcinoma of the uterus was removed seventeen years before examination, with no subsequent difficulty. Since menopause at the age of 55, she had felt a small hard lump in the right breast which was diagnosed as a "hardened milk duct." The lump was traumatized four years before examination and had since gradually increased in size. Two years later, a mass appeared in the right axilla followed by pain in the breast. One year prior to examination the cancer in the breast ulcerated and for the first time swelling of the hand and arm appeared. Figure 4 shows the ulcerative mammary carcinoma.

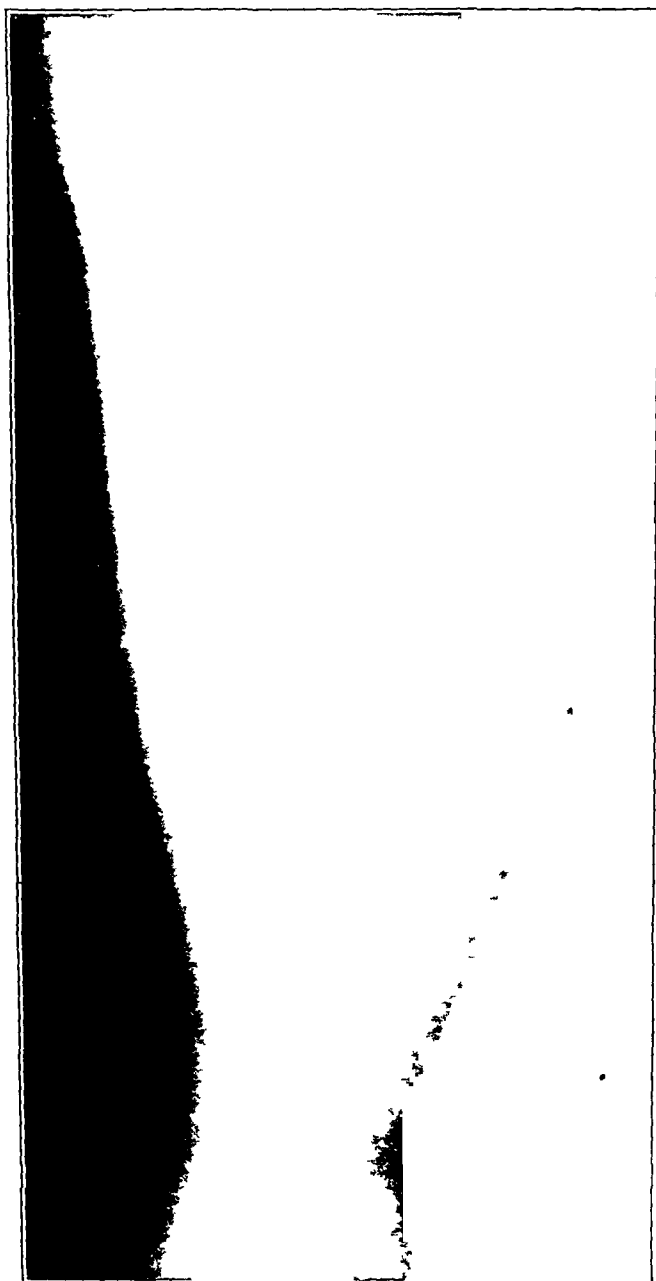


Fig 3 (case 1)—Soft tissue roentgenogram to show diffuse homogeneous cloudiness throughout the swollen leg typical of vascular edema

with a large, hard, axillary metastasis firmly attached to the skin and deeper structures. The entire right upper extremity was enlarged and indurated. Although the right and left arms appeared to be of about the same size, the right was much heavier and felt boardlike, with a thick leathery skin and an indurated hypodermal layer. This enlargement of the extremity appeared only after the carcinoma had ulcerated and become infected. No history of an elephantiasic fever could be obtained.

A diagnosis of elephantiasis of the extremity was made and was confirmed by the soft tissue roentgenograms (figs 5 and 6). In order to make a reproduction similar to the original roentgenogram and to prevent loss of detail, the photographic reprints have been retouched. Dr R. R. Newell's report of the roentgenograms is as follows: Both arms were very large. There was a rather marked

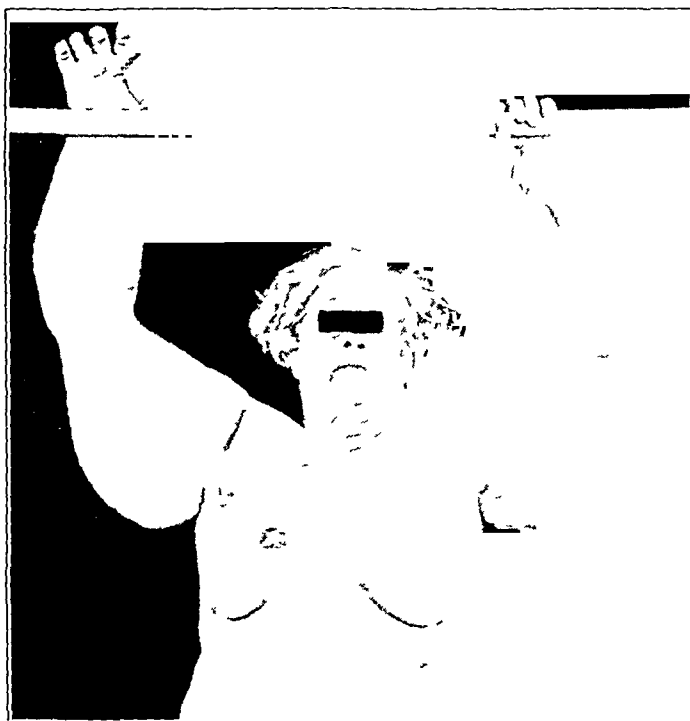


Fig. 4 (case 2) —Right ulcerated mammary carcinoma, with axillary metastasis and elephantiasis of the right upper extremity.

contrast in the appearance of the two, however. The consistency of the left was rather smooth. The muscles could be seen overlying the bone, and in the very thick fatty layer branched vessels could be traced quite clearly. He believed that he could identify the cephalic and basilic veins. The consistency of the subcutaneous layer in the right arm was different, however, being markedly reticulated. The directions of the fibers were irregular, but on the whole were rather at right angles than parallel to the humerus. On account of these reticulae and the slightly greater density, the veins did not stand out as clearly as they did in the left arm. The forearms showed the same contrast in the appearance of the soft parts as did the upper arms, but in much more marked degree. Trabeculation of the subcutaneous tissue in the right arm was very coarse and heavy, on the whole it was irregular in orientation, but was inclined to be arranged vertical to the length of

the arm rather than parallel to the surface of the skin. No definite changes in the bone were made out, except for some sharpening of the left coronoid, attributed to chronic arthritis.

CASE 3—H. M., a woman, aged 63, had suffered from varicose veins in the right leg for the past forty-eight years, and for several decades eczema had persisted on the medial surface of the leg. Three years before examination the eczematous area was severely scratched and an ulcer formed. No swelling of the leg was noted at that time. In another hospital, the ulcer was treated by compresses followed by varicotomy. The convalescence was stormy, with fever and



Fig 5 (case 2)—Retouched print of soft tissue roentgenograms of the right and left arms. Although of about the same size the right arm shows the typical trabeculations in the subcutaneous layer characteristic of elephantiasis.

bilateral pleurisy and the limb became swollen and painful. She was unable to walk for three months and since then the leg and thigh had remained swollen with persistence of the edema. One year prior to examination, because of pain and redness in this limb an incision was made for pus, but the diagnosis was given as *Streptococcus cellulitis*. The eczema continued uncontrolled, with frequent small excoriations. The extremity had gradually enlarged, with the development of a brown edema and a thick leathery skin as shown in figure 7.

The diagnosis of elephantiasis of the right lower limb was confirmed by the soft tissue roentgenograms (fig 8).

CASE 4—W T, a woman, aged 47, following a laceration of the left leg thirty-two years before examination, suffered from considerable swelling and inflammation which remained for a few weeks. Four years later a more or less continuous edema first appeared, and since then she had suffered from several attacks of local inflammation in the leg attributed to scratches or trauma. At the age of 39, following pregnancy the enlarged superficial veins in that limb became thrombosed followed by greater swelling of the leg. Two years before examination, after an attack of "blood poisoning" in the leg, an ulcer appeared on the skin and the edema became more severe. Although the ulcer healed she had had seven or eight subsequent inflammatory attacks, the last one being diagnosed as erysipelas. All of these were initiated by malaise, chills and fever, nausea and vomiting and red-



Fig 6 (case 2)—Retouched print of soft tissue roentgenograms of the right and left forearms. A very coarse and heavy subcutaneous trabeculation is present in the elephantiasis forearm.

dening of the skin of the leg with intense itching. After each attack the limb was heavier and more painful, and the skin was thick and hard to dent. The patient was seen at the end of the last attack, during which the reddish eruption and erythema had spread upward to the left groin and on the upper part of the right thigh. The entire left extremity was markedly swollen, red and hot. The skin and subcutaneous layer were indurated and twice as thick as on the right side.

A diagnosis of elephantiasis with elephantoid fever was made. This was substantiated by the appearance of the soft tissue roentgenograms (fig 9).

CASE 5—H T, a man, aged 73, five years before examination noticed a small wartlike growth on the sole of the right foot which gradually increased in size.

Two years later, this cancerous growth was excised, and the area was grafted with the Thiersch graft. Six months later the wound broke down, with a recurrence of the tumor accompanied by chills, fever and swelling of the leg. Infection continued, and the foot and leg remained swollen. Recently, enlarged inguinal glands were felt. The lower leg showed brawny induration of the skin and underlying tissues, but this did not extend into the enlarged thigh (fig 10).

The diagnosis was infection of recurrent epithelioma of the foot, with an elephantoid condition of the foot and lower leg. Soft tissue roentgenograms (fig 11) showed considerable trabeculation of the thickened hypodermal tissue especially marked in the lower half of the right leg.

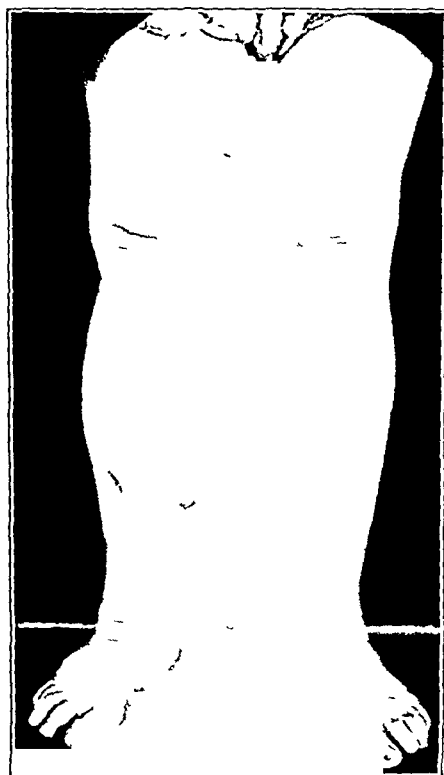


Fig 7 (case 3)—Elephantiasis of the right lower limb in a patient with a history of varicose veins, eczema of the leg and attacks of lymphangitis.

CASE 6—D. S., a man, aged 57, had been troubled with bilateral varicose veins for a number of years. An eczematous condition of the skin led to ulcerations on both legs. On the right, the ulcer healed for a time, and when first seen there was an old, pigmented, indurated scar on the right leg while the ulcer on the left leg, which had resisted all manner of treatment for twelve years, measured 5 by 3.5 cm. The tissues about the ulcer were indurated and firm, in places boardlike to palpation, with an edema involving the knee and thigh. Large tortuous varicose veins were seen on both limbs. After two months of treatment in the outpatient clinic the ulcer measured 3 by 2.5 cm and then became larger. The patient was then hospitalized (fig 12). At this time soft tissue roentgenograms showed some



remarkable calcifications in the legs and considerable irregular trabeculation in the subcutaneous tissues, more marked on the left

After the ulcer was treated with surgical solution of chlorinated soda, the varicose veins were thrombosed by injections of hypertonic saline solution and small deep skin grafts were applied to the ulcerated area. A month later, a photograph (fig 13) showed the healed ulcer with a diminution in edema and absence of varicose veins. Four months later, the elephantoid condition was greatly improved, the tissues were considerably softer with no evidence of edema and the ulcer remained healed.



Fig 8 (case 3) —Retouched print of soft tissue roentgenograms of both legs, with the heavily reticulated hypodermal layer on the right side indicative of elephantiasis

#### TREATMENT

From the previous discussion of elephantiasis and elephantoid conditions and a study of the case reports, one is struck by the relative frequency of these conditions and by the fact that through neglect or carelessness they have been allowed to develop on the common and often readily remedied disturbances of the venous and lymphaticovenous systems.

The importance of preventive measures is clearly indicated. Varicose veins are the precursors of distressing edema, indolent ulcers, painful indurations and, finally elephantoid states. Once infection appears, hyperplasia of the connective tissue elements is sure to follow and is difficult to eliminate without radical surgical measures. So, too do the chronic bacterial, fungoid and malignant ulcerations lead to the same sequelae with either an elephantoid state or elephantiasis as the



Fig 9 (case 4) —Retouched print of soft tissue roentgenograms of both legs of a patient with a history of varicose veins and ulcer and recurrent attacks of elephantiasis fever in the left lower extremity. There are marked hypodermal trabeculations in the affected limb. (From *California & West Med* **31** 233 [Oct] 1929.)

final result. As Homans<sup>11</sup> emphasized more care must be exercised in the early treatment for phlegmasia alba dolens if one is to prevent the later development of elephantiasis.

The recently popularized method of obliterating varicose veins by means of sclerosing solutions affords an ambulatory treatment for this

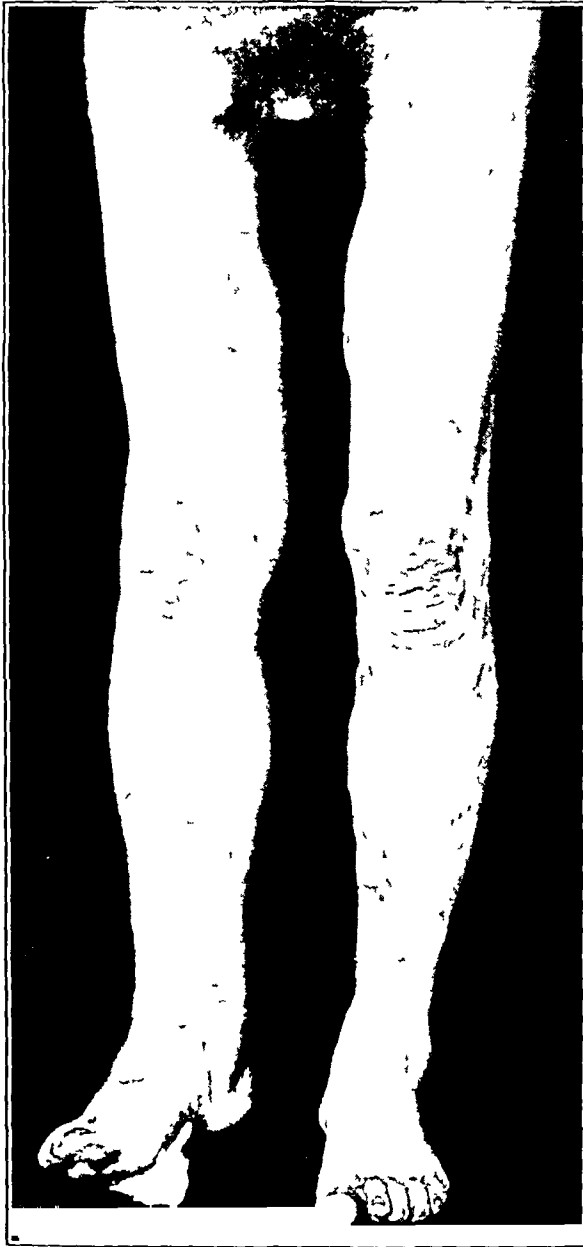


Fig 10 (case 5) —Patient with infected malignant ulceration on the sole of the foot with inguinal metastasis, enlargement of the whole right extremity and an elephantoid state in the foot and lower leg

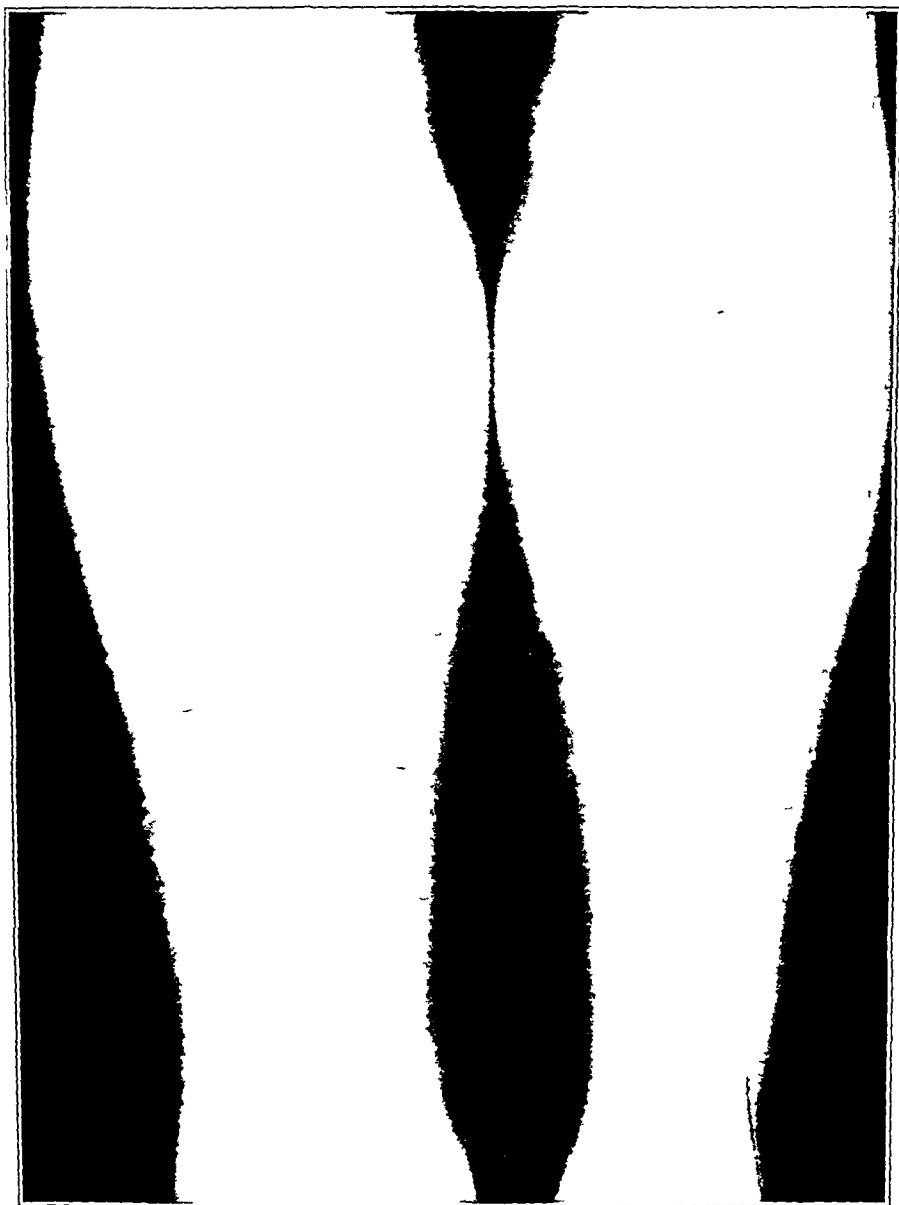


Fig 11 (case 5) —Untouched print of soft tissue roentgenograms of both legs showing the heavy trabeculations of an elephantoid condition in the lower half of the right leg

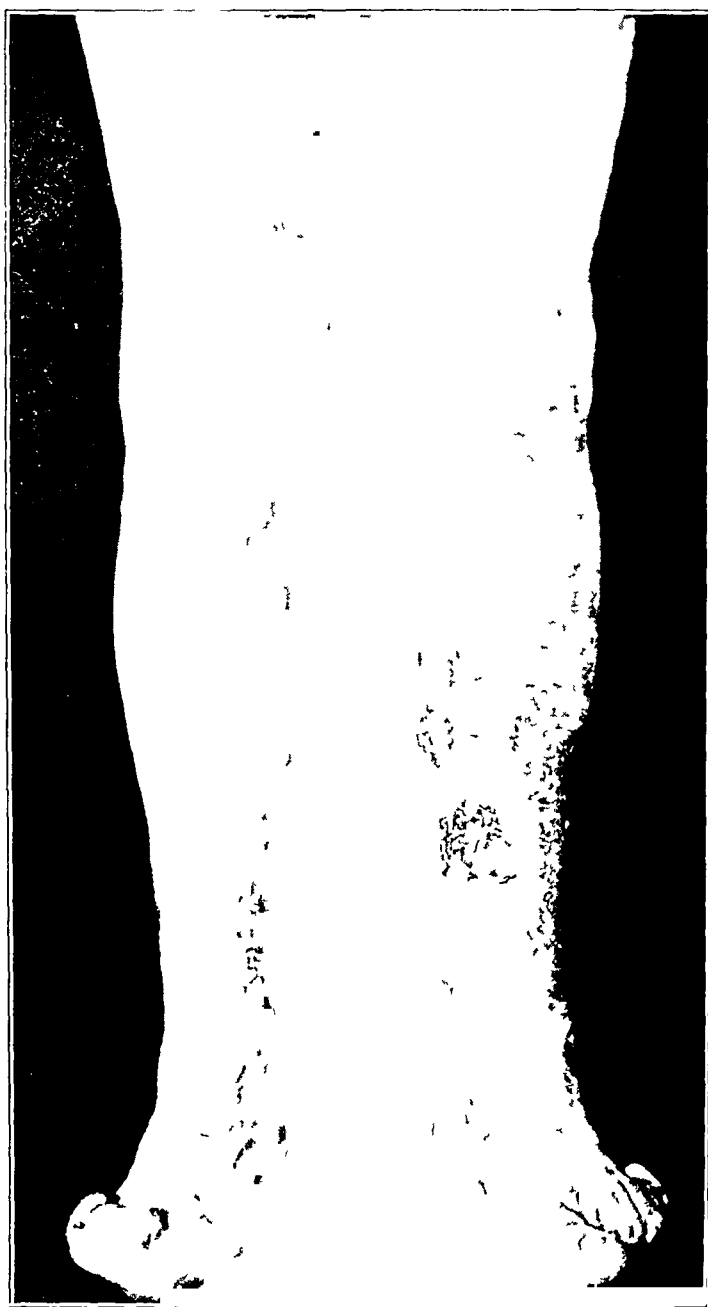


Fig 12 (case 6) —Patient with bilateral varicose veins and chronic ulcer on the left leg of twelve years' duration

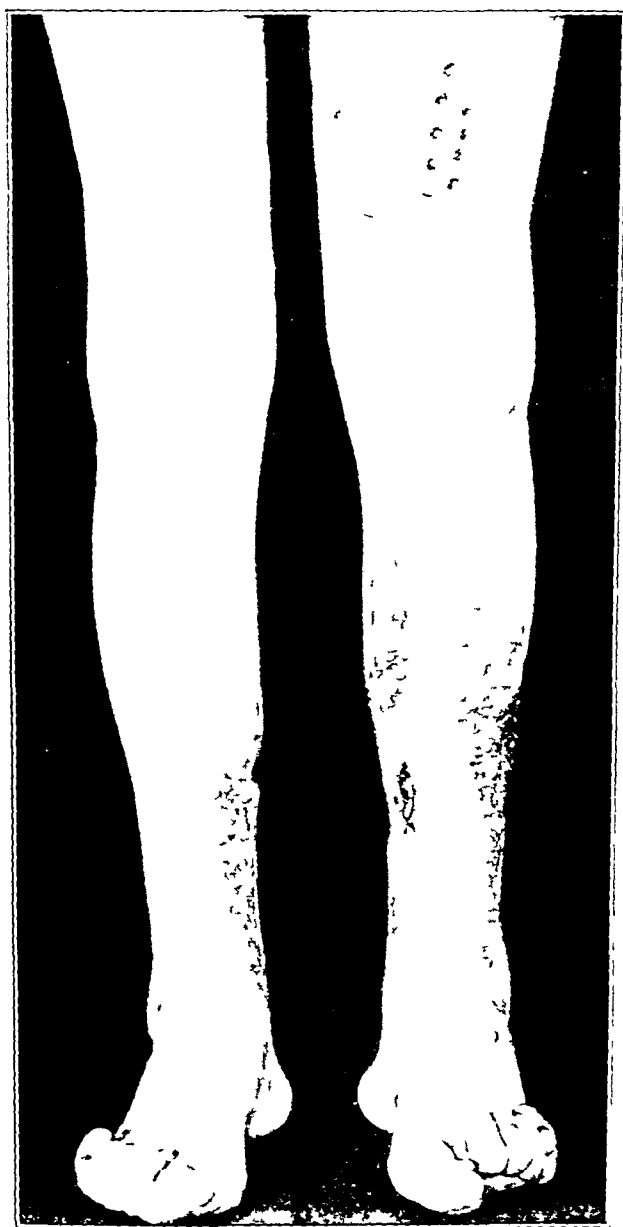


Fig 13 (case 6) —Patient one month after thrombosis of the varicose vein- and epithelization of the ulcer on the left leg showing marked improvement in the edema and elephantoid condition

condition, to which patients readily consent, and in this way the incapacitating sequelae can be prevented. Patients with ulceration need immediate care directed to the healing of the ulcer and obliteration of the veins, for the longer the ulcer persists the more the fibromatosis develops and the limb remains in a potential elephantoid state. At times the base of the indolent ulcer is so indurated and devitalized that skin grafting is unsatisfactory unless excision of the ulcerated and fibrosed area and the thickened underlying aponeurosis is resorted to, as advocated by Homans and Traut.

For the late complications of phlegmasia alba dolens, Homans reported some success in overcoming the persistent swelling by the excision of strips of deep fascia for some distance above and below the edema. When the tissues are indurated or ulcerated, he included the fascia of the muscle in the excision.

Of utmost importance is the prevention of infection in a limb edematous from derangement of the lymphaticovenous system. Eczematous regions must be carefully treated and other areas of focal infection must be eradicated in order to eliminate the recurrent attacks of fever and lymphangitis. Vaccine therapy and injections of antistreptococcal serum have been used to advantage and have frequently aborted further attacks of elephantiasis fever.

As to the methods of treatment for elephantiasis, the best results are obtained by surgical procedures. Matas<sup>5</sup> gave an historical resumé of the surgical treatment and expressed the belief that the Kondoleon procedure is the most encouraging. Beitwistle and Gregg<sup>7</sup> agreed that the Kondoleon operation offers a good prospect of prolonged temporary, if not permanent, cure. After ten years of experience with this operation, Sistrunk<sup>15</sup> expressed the belief that it is of much value in dealing with this disease, his admirable illustrations perhaps describe the operation better than words.

Kondoleon<sup>16</sup> devised the operation in order to reestablish connections between the deranged superficial lymphatic system and the uninvolved deeper set of lymphatics. By removing a large amount of aponeurosis covering the muscles, he hoped that connections would be established between the two lymphatic systems. At the same time a large amount of skin and subcutaneous tissue was removed to decrease the size of the limb, and then the edges of the skin were approximated. This procedure was accomplished in several stages on both sides of the thigh and leg.

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15 Sistrunk, W. E. Contributions to Plastic Surgery. The Kondoleon Operation for Elephantiasis, *Ann Surg* 85 185 (Feb) 1927.

16 Kondoleon, E. Die Lymphableitung, als Heilmittel bei chronischen Oedemen nach Quetschung. *München med Wchnschr* 59 525 (March 5) 1912.

No proof is available that connections are established between the two sets of lymphatics by this operation, and that it is this regeneration and refunctioning of the superficial lymphatic group that leads to the marked improvement following this operation. Examination of several of these cases five and six years after operation strongly suggests that this improvement is largely due to the mechanical removal of a great amount of the diseased tissue namely, removal of the skin subcutaneous tissue and muscular aponeurosis the only structures pathologically involved in this condition.

#### SUMMARY

The lymphatics, as a system of vessels and capillaries are considered as objective and definite as the arteries and veins, and their growth and regeneration normally as well as in the presence of scar tissue is similar to that of the vascular system. Their importance in the maintenance of circulatory balance is emphasized.

True lymphedema is differentiated from vascular or pitting edema by its restriction to and induration of the skin and subcutaneous tissues. No edema even of long duration will lead to a proliferative change and deposition of fibrous connective tissue.

Elephantiasis is caused, not by lymph and venous stasis alone but by its association with inflammation due to infection or toxemia. Chronic inflammatory fibromatosis of the dermal and hypodermal connective tissue is characteristic of this condition. The element of inflammation is the one essential factor in the production of elephantiasis. Elephantiasis tropicum, elephantiasis nostras streptogens and the elephantiasis chirurgica of Halsted all have the same pathologic background and differ only in the primary cause of the lymphatic and venous stasis.

The experimental work showed the importance of the lymphaticovenous system in maintaining circulatory balance. The production of lymphedema and lymphaticovenous stasis occurred in replanted limbs as well as by venous and perivenous blockade. Only one step the induction of lymphangitis, apparently remains in obtaining experimental elephantiasis.

Elephantoid conditions are frequently seen, and emphasis is again placed on the importance of their recognition. The elephantoid state is a frequent sequel to varicose veins and phlegmasia alba dolens and to chronic bacterial, fungoid and malignant ulcerations.

Soft tissue roentgenograms of an extremity present a characteristic picture in elephantiasis and elephantoid conditions and serve as an adjunct in diagnosis and prognosis. The roentgenographic trabeculation in the hypodermal layer is produced by the fibromatosis in this tissue.



A few selected cases with their soft tissue roentgenograms serve to illustrate simple edema elephantiasis and elephantoid states

The importance of prophylactic measures is clearly indicated in the treatment for these conditions. In addition to preventive methods, such as the obliteration of varicose veins and epithelization of ulcers, the treatment for elephantiasis and elephantoid states by the Kondoleon procedure and its modifications is discussed

# GELATINOUS CARCINOMA OF THE BREAST<sup>\*</sup>

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Gelatinous carcinoma<sup>1</sup> of the breast is a comparatively rare state. In a combined group of 2,944 carcinomas of the breast cited by Gaabe,<sup>2</sup> 49, or 1.66 per cent, were of the gelatinous type. Gelatinous carcinoma occurs in patients of about the same age as do the usual forms of carcinoma of the breast. Tumors undergoing gelatinous degeneration sometimes reach an enormous size and the mass of the tumor may consist largely of gelatinous material. On the other hand, the amount of gelatinous material may be so small that it may be readily overlooked. Similar degeneration is known to occur in tumors arising in other situations where mucin-forming cells abound, notably the large intestine, stomach and biliary tract.

Gelatinous carcinoma of the breast exhibits characteristic gross and microscopic appearances. The gross features may be striking. Large or small areas of the tumor may be somewhat translucent in appearance and may either consist of a light gray jelly-like substance or be light reddish brown. The gelatinous material may appear delimited by a more or less irregular outline. In the advanced stages, small and large tumors may fail to show any solid unaffected structure, the entire mass consisting of gelatinous material. On account of the innocent appearance of the lesion under these particular circumstances, an entirely false conception of the true state of affairs may be obtained from macroscopic examination alone.

Microscopically, gelatinous carcinoma of the breast has the usual appearance of carcinoma in addition to which islands of degenerating and necrotic epithelial cells can be seen amid diffuse areas of gelatinous material. This material is typical in arrangement and appearance and requires no special stain in order for its presence to be detected. If a stain is desired, either mucicarmine or neutral red is appropriate.

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<sup>\*</sup> Submitted for publication Dec 10, 1929.

<sup>1</sup> The terms "colloid carcinoma" and "mucoid carcinoma" are also applied to this condition.

<sup>2</sup> Gaabe G. Der Gallertkrebs der Brustdrüse, Beitr z klin Chir 60 760, 1908.

The prevailing opinion regarding gelatinous carcinoma of the breast is that it is the least malignant form of mammary carcinoma. According to this opinion, the disease is slower in its course, metastases occur later and the prognosis is more favorable than in the usual type. With few exceptions, the conception that this form of the disease may be highly malignant is not encountered in the literature. Several authors, however, have drawn attention to the highly malignant nature of some of these tumors (Despres,<sup>3</sup> Schmidt,<sup>4</sup> Gaabe<sup>2</sup>). Others, notably Lange,<sup>5</sup> while regarding these tumors as less malignant, admitted that the ultimate prognosis is not more favorable than in other types of carcinoma of the breast.

The first pathologic description of gelatinous carcinoma of the breast was attributed by Gaabe to Otto in 1816. The origin of gelatinous material in carcinoma of the breast is still the most interesting and disputed phase of the disease. The subject has been a matter of controversy since the condition was first recognized. Doutrelepon and Rindfleisch<sup>6</sup> attributed the formation of the gelatinous substance to an exudation of the blood plasma through the blood vessels with subsequent diffusion of the exudate into the tumor, a formation analogous to the process of edema. The chief point of dispute among pathologists is the question whether the connective tissue stroma or the epithelial cells of the tumor give rise to the gelatinous substance. The belief that the gelatinous substance originates in the connective tissue stroma has been held by Virchow, Meyer,<sup>7</sup> Kaufmann<sup>8</sup> and others. Lange was the first to study this problem by the use of a special stain (toluidinblau) and concluded that the origin of gelatinous material varied in tumors of different organs. In gelatinous carcinoma of the gastro-intestinal tract, he described a diffuse degeneration of the protoplasm of the tumor cells. In gelatinous carcinoma of the breast, the gelatinous degeneration occurred in the connective tissue, the tumor cells taking no direct part in the process. Lange's observations concerning the connective tissue origin of the gelatinous material were supported by Kaufmann who, on the basis of a study of five cases, reached a similar conclusion. From a study of four cases Ewing<sup>9</sup> concluded that the gelatinous degeneration

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3 Despres. *Traité du diagnostic des maladies chirurgicales*, Paris, 1886 p 272

4 Schmidt, G. B. *Diese Beiträge* vol 4, 1888

5 Lange F. *Der Gallertkrebs der Brustdrüse*, vol 16, 1896

6 Doutrelepon und Rindfleisch. *Arch f klin Chir* 12 551, 1870

7 Meyer. *Beiträge zur Histologie der schleimbildenden Adenome und Carcinome der Brustdrüse*, Diss. Rostock, 1880

8 Kaufmann, E. *Lehrbuch der speciellen pathologischen Anatomie* ed 3 1904 p 958

9 Ewing. *Neoplastic Diseases* Philadelphia, W. B. Saunders Company 1928

had involved and partly originated in the fat tissue in the stroma Borst<sup>10</sup> believed in a double origin from connective tissue and epithelial cells

The notion that the gelatinous substance is the exclusive product of the epithelial cells is held by numerous authorities Ribbert<sup>11</sup> noticed that in the early stages mucoid secretion begins in the lumen of the acini whence it breaks through and infiltrates the surrounding connective tissue Zimmermann<sup>12</sup> stated that the gelatinous substance was an epithelial cell product and pointed out the possible fallacies in the interpretation of reactions to special stains as performed by Lange Finally Gaabe concluded that in most gelatinous carcinomas of the breast, the gelatinous substance begins as a degeneration and subsequent destruction of epithelial cells without any active participation of the connective tissue A gelatinous carcinoma of the breast with laminated calcified masses scattered through the tumor was depicted by Delafield and Prudden<sup>13</sup>

The comparatively slow growth of gelatinous carcinoma of the breast was first pointed out by Lebert,<sup>14</sup> who described two cases in which the disease had lasted ten and twelve years, respectively This observation was soon confirmed by Simmonds,<sup>15</sup> who reached similar conclusions after a study of twenty cases The most extensive study of this subject was made by Lange<sup>5</sup> in 1896 when he reported seventy-five cases and by Gaabe in 1908, whose report comprised a study of sixty-nine cases of this form of carcinoma of the breast Lange concluded that gelatinous carcinoma of the breast is more benign, grows more slowly and metastasizes more rarely than the usual forms of carcinoma of the breast He pointed out the special tendency to late recurrence but concluded that the ultimate prognosis after operation is scarcely more favorable than in the usual forms of carcinoma of the breast Gaabe's conclusions are essentially similar to those of Lange His study of sixty-nine cases showed that gelatinous carcinoma of the breast differs from the usual type of carcinoma of the breast in the following ways (1) the rate of growth is slower (2) the invasion of skin, muscles and axillary glands and the development of ulceration occur two and one-half times as late (3) recurrences appear later, and (4) the results

10 Borst *Geschwulstlehre*, Wiesbaden, 1902

11 Ribbert *Geschwulstlehre* Bonn 1904

12 Zimmermann *Ueber seltenere Formen der Brustdrüsen-geschwulste*, Diss., Strassburg 1902

13 Delafield and Prudden (revised by F C Wood) *A Textbook of Pathology* ed 14, New York William Wood & Company 1928

14 Lebert *Virchows Arch f path Anat* 1852 vol 4

15 Simmonds *Deutsche Ztschr f Chir*, vol 20 p 74

of operation are at least twice as favorable, the operative cures being 51.43 per cent in gelatinous carcinoma against 25 per cent in the usual forms of breast carcinoma.

The fact that this form of the disease may be highly malignant is greatly obscured in the literature. Two references to this possibility, however, could be discovered. Despres<sup>3</sup> and Schmidt<sup>4</sup> pointed out that these tumors may be highly malignant and Gaabe stated that a gelatinous carcinoma may lose its gelatinous characteristics; its cells take on a high grade of anaplasia and the tumor may revert to a carcinoma of the usual type.

#### REPORT OF EIGHT CASES

**CASE 1—Clinical History**—A woman, aged 43 years, married, with two children, while in South Africa in July, 1928, noticed a painful lump in the right axilla which was rapidly increasing in size. At that time there were no clinical signs in the breast. The axillary mass was excised and on microscopic examination was found to contain carcinoma in a state of gelatinous degeneration. The patient was sent to London, where she was seen in consultation by one of us (G. L. C.) and by Mr. S. Cade (October, 1928). The breasts were very fat, there were no clinical signs of a tumor in the right breast, and no enlarged glands could be discovered in the right axilla and supraclavicular regions. There was no history of a discharge of blood from the nipple. A complete operation was performed on the right side. As a tumor could not be detected in the breast either before or after removal, whole microscopic sections of the gland were cut. Three months after the operation the patient returned with an extensive local recurrence in the skin and subcutaneous tissue. Mr. S. Cade treated the recurrence by means of external irradiation. The irradiation was followed by rapid and complete disappearance of the tumors. The regression was that of a highly radiosensitive tumor. The whole of the chest and mediastinum was subsequently treated with high voltage roentgen rays as a prophylactic measure by Dr. Finzi.

**Pathologic Examination**—Figure 1 illustrates the whole microscopic section in which the lesion was discovered. At *B* a carcinomatous patch which had undergone gelatinous degeneration was discovered. Diffuse carcinomatosis in ducts and acini existed throughout the whole of this area of the gland. At *C* there was a dilated duct in which the tumor had undergone gelatinous degeneration. Figure 2 shows this duct magnified. The epithelial neoplasia within the affected ducts and acini and outside them exhibited the characteristic morphologic appearance of anaplasia. The growth was diffuse, the cells were small and highly atypical and mitoses were abundant.

We wish at this point to call special attention to the presence of two distinct types of malignant epithelial cells in this tumor. One type belongs to the common spheroidal cells, the other type presents morphologic features which differ from the usual appearance of anaplastic epithelial cells. The cells are somewhat larger, the nuclei stain darkly, vary in size and shape, are relatively small and may occupy the center of the cell, or they may be eccentric. The cytoplasm is acidophilic and homogeneous and has well defined margins. The staining characteristics of the cytoplasm, the shape of the cells and the eccentric position of the nucleus give to some of the cells an appearance like that of a "plasma cell." They differ from plasma cells by being much larger. They possess the same degree of malignancy as the usual type of anaplastic cell, growing diffusely, dividing rapidly and infiltrating widely in small groups and singly.

No further involvement of axillary lymphatic glands was discovered by microscopic examination although the lymphatic glands that were removed at the first operation contained extensive carcinoma which had undergone gelatinous degeneration

*Comment*—The inability to discover any tumor in the breast in case 1 on clinical examination may be accounted for in two ways (1) by the adiposity of the breast, the layer of subcutaneous fat having

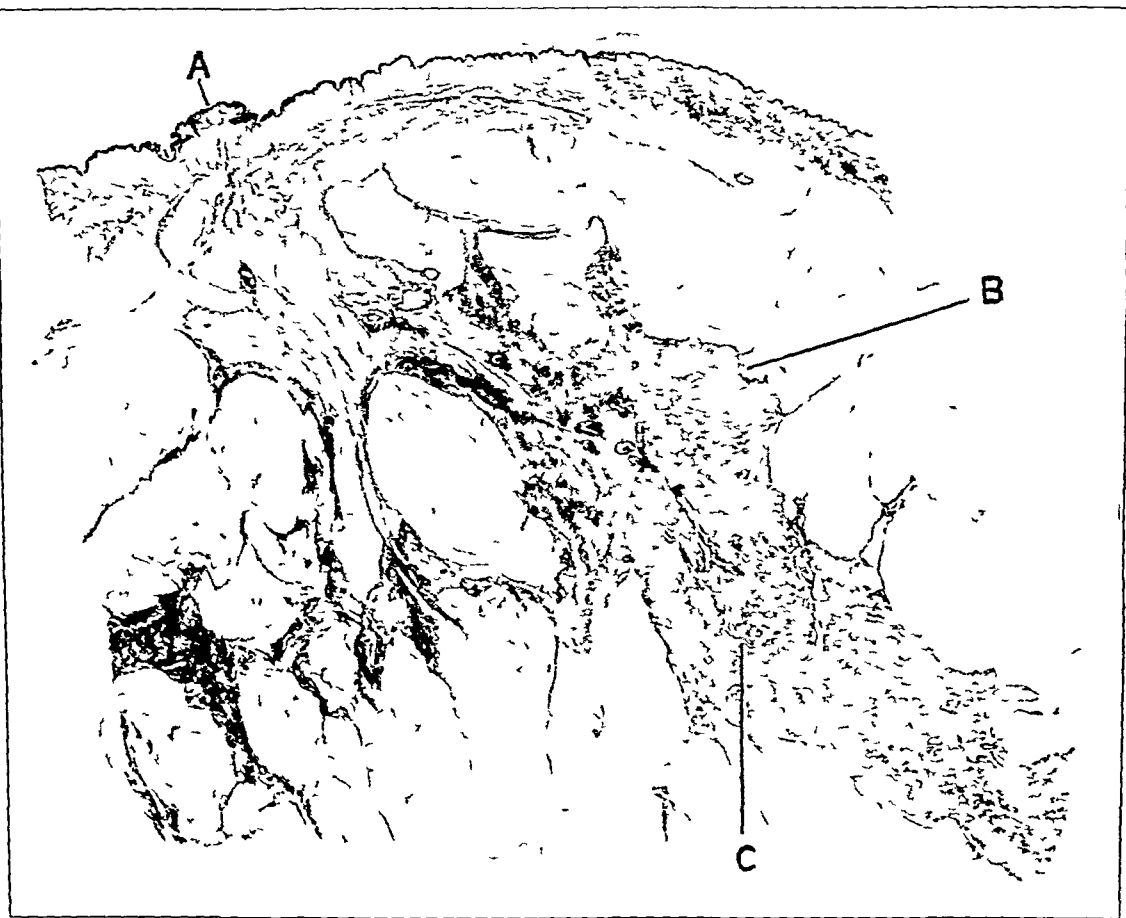


Fig 1 (case 1)—Whole microscopic section of breast. *A* nipple, *B* site of gelatinous tumor, *C* situation of duct, a high power magnification of which is shown in figure 2. The examination of these photomicrographs can be greatly assisted by using a hand lens. By this means the more minute details can be observed.

measured 3 cm in thickness and (2) by the fact that the carcinomatous parts adapted themselves to the contour of the breast and therefore their presence was obscured on palpation. In fact it was necessary to cut numerous serial sections of this gland before the tumor could be discovered. The size of the lesion is to a great extent accounted

for by the fact that an extensive and diffuse malignant epithelial neoplasia existed within the ducts and acini. In the duct shown here (fig. 2) the hyperplasia had undergone gelatinous degeneration. We regard the presence of gelatinous degeneration of the epithelial neoplasia within the duct as evidence in favor of our conviction that the epithelium can be carcinomatous even though it is still confined within normal boundaries. This belief is supported by the fact that the cells within the ducts that had not undergone gelatinous degeneration were in a highly anaplastic state. The first sign of disease was an enlargement



Fig. 2 (case 1) —Magnification of duct shown in figure 1. *C* Gelatinous degeneration has occurred in the epithelial neoplasia with which it is filled. The same change is occurring in the acini *C* into which it branches. The elastica, unstained in this section, has undergone a slight degree of hyperplasia.

of an axillary lymphatic gland and there were no clinical signs of a tumor in the breast. Finally, it is necessary to draw attention to the marked radiosensitivity of this highly anaplastic tumor. In this example the intimate relationship that existed between the anaplastic histologic structure, the high degree of malignancy indicated by its early metastasis to a lymphatic gland and its marked radiosensitivity were completely demonstrated.



Fig 3 (case 2) — 1 ducts and dilated acini, some of which have become confluent B, the epithelial elements in these structures consist of small round cells, crowded together with no definite arrangement which are highly anaplastic in type



Fig 4 (case 2) — At A is a dilated acinus in which gelatinous degeneration has occurred in the epithelial cells which fill and distend the structure giving rise to a honeycomb appearance. At B the neoplastic epithelial contents of a duct are in an advanced stage of gelatinous degeneration



**CASE 2—Clinical History**—A married woman, aged 44, with one child, noticed a tumor in the right breast eighteen months before operation. During this period she had been treated in India for "chronic mastitis." The breast was painful and there had been no discharge of blood from the nipple. Examination of the right breast revealed a large tumor 5 by 3 by 3 cm. occupying the outer middle segment. The mass was firm and nodular, and puckered the skin. The nipple was movable and not retracted. The axilla was filled with large, firm and discrete lymphatic glands. The supraclavicular glands were not palpable. The opposite breast and axilla were normal. Radical operation was performed. The patient died with visceral metastases nineteen months after the operation.

**Pathologic Examination**—At least two ducts in immediate juxtaposition were full of epithelial neoplasia extending from immediately beneath the nipple into



FIG 5 (case 2)—*A*, longitudinal section of a duct showing gelatinous degeneration of the epithelial cells within it. *B* and *C*, epithelial cells within acini undergoing gelatinous degeneration. The elastica of the duct has not been stained in this specimen but other sections show that it has undergone slight hyperplasia.

all their acini. One of these ducts, its branches and its acini could be traced with only slight interruptions throughout the whole course of its distribution. The other duct was not so completely demonstrated and only its beginning beneath the nipple could be seen. The chief mass of this tumor was due to epithelial neoplasia that was confined within the normal boundaries of the ducts and acini and epithelial invasion could be detected in only two places. The morphologic appearances of the epithelial neoplasia varied in different parts. In the terminal ducts and acini the cells were elongated and tapered. In some ducts papillomas had

formed with delicate stalks of connective tissue. Some terminal ducts and acini were distended by epithelial cells that were highly anaplastic in type (fig 3 *A*). Within other ducts and acini the epithelial cells were arranged in a laciform manner (fig 4 *A*). This peculiar formation was due to the gelatinous degeneration of epithelial cells, which caused the spaces among the remaining and unaffected parts. Gelatinous degeneration could be seen occurring in a more advanced state in many other isolated parts (figs 4 *B* and 6 *A*). Most of the tumor had not undergone gelatinous degeneration. Gelatinous degeneration had occurred in the neoplastic epithelium contained in the duct shown in figure 5 *A*, and in the beginnings of two ducts beneath the nipple. The elastica had not undergone hyperplasia and was normal in amount and distribution. The glands in the axilla were extensively affected by carcinoma and had not undergone gelatinous degeneration. Carcinoma had extended beyond the upper border of the first rib and the operation was unsuccessful in reaching the limits of the disease.



Fig 6 (case 2) —*A*, gelatinous degeneration occurring in epithelial cells after they have invaded outside tissues, *B*, connective tissue which does not show any gelatinous degeneration

*Comment*—Except that the disease was more advanced in this tumor, it resembles that in case 1. The distribution of epithelial neoplasia confined within the ducts and acini was extensive in both specimens. It is remarkable that in so large a tumor there were so few sites of epithelial invasion of the stroma, especially when the lymphatic glandular involvement was so extensive. The explanation lies in the highly anaplastic state of the epithelial neoplasia in some parts of the tumor. The normal appearance and distribution of the elastica enabled us to trace the ducts and the acini and so to confirm our statement that the epithelial neoplasia continued within normal but distended boundaries.

formed the main mass of the tumor. Microscopic examination of this tumor showed that the neoplastic epithelium was the first to undergo gelatinous degeneration and that this degeneration could begin in epithelial neoplasia when confined within normal boundaries. The laciform appearance of the neoplastic epithelium in parts of this tumor was due to the gelatinous degeneration of epithelial cells. A laciform appearance occurring in other carcinomas may be due to the union of anastomosing columns of epithelial cells or to a different type of degeneration occurring among them. The history of the patient demonstrates



Fig 7 (case 3) —Portion of a whole microscopic section. The ducts and acini are seen distended with neoplastic epithelium which in the duct *A* and its branches *B* and *C* have undergone gelatinous degeneration. The clastica, unstained in this section, has undergone a slight degree of hyperplasia.

the prevalent danger of trusting to a diagnosis of so-called chronic mastitis.

**CASE 3—Clinical History**—A woman, aged 38, married, with two children, was sent home from India with a tumor about 2.5 cm. in diameter situated in the lower and outer segment of the right breast. This tumor had been noticed for about three months and was causing a localized stinging pain. It was gradually increasing in size. There was no discharge from the nipple. On examination the skin puckered, the nipple was normal and the tumor was hard, nodular and freely movable. There was an enlarged discrete hard and tender lymphatic gland

beneath the outer border of the pectoralis major. There was no other adenopathy in the axilla or supraclavicular regions. The opposite breast was normal.

*Pathologic Examination*—Microscopically the lesion was more extensive than the clinical signs indicated. Figure 7 shows part of a whole microscopic section of the breast that was cut in a vertical plane parallel with the anterior surface of the body. Its general shape was triangular with the apex toward the nipple. Although the main mass of the tumor was due to the presence of the epithelial neoplasia that was contained within the normal boundaries of the ducts and acini, there was also considerable epithelial invasion of the outside tissues. The epithelial neoplasia was not anaplastic in any part of the tumor. With this exception, it resembled the two tumors just described. Gelatinous degeneration was advanced in some parts of the tumor where cellular invasion had occurred. In other parts,



Fig 8 (case 3) —Another duct in which the neoplastic epithelial content has undergone gelatinous degeneration.

the gelatinous degeneration was in an advanced state while still confined within the normal boundaries of the ducts and acini (figs 7-4 and 8). The elastica had not undergone hyperplasia and was normal in amount and distribution. The lymphatic gland in the right axilla was the only one affected and the carcinoma it contained had not undergone gelatinous degeneration.

*Comment*—This specimen is another example of the wide distribution of malignant epithelial neoplasia that can be confined within normal boundaries. It also demonstrates gelatinous degeneration of epithelial neoplasia while it is thus confined and shows that the gelatinous degeneration in its early states begins in the epithelium. It is an example of

gelatinous degeneration occurring in a carcinoma, the epithelium of which is not anaplastic. In this respect, it differs from the former two cases. This case also demonstrates that the primary lesion in the breast may be much more extensive than the clinical signs suggest. The patient is well and apparently free from disease five years after operation. In this respect it is interesting to point out that the tumor was not highly anaplastic, which probably accounts for the patient's present condition, even though one axillary lymphatic gland had been involved in the disease.

*CASE 4—Clinical History*—A married woman, aged 43, noticed a lump in the right breast six months before operation. On examination there was a hard, round

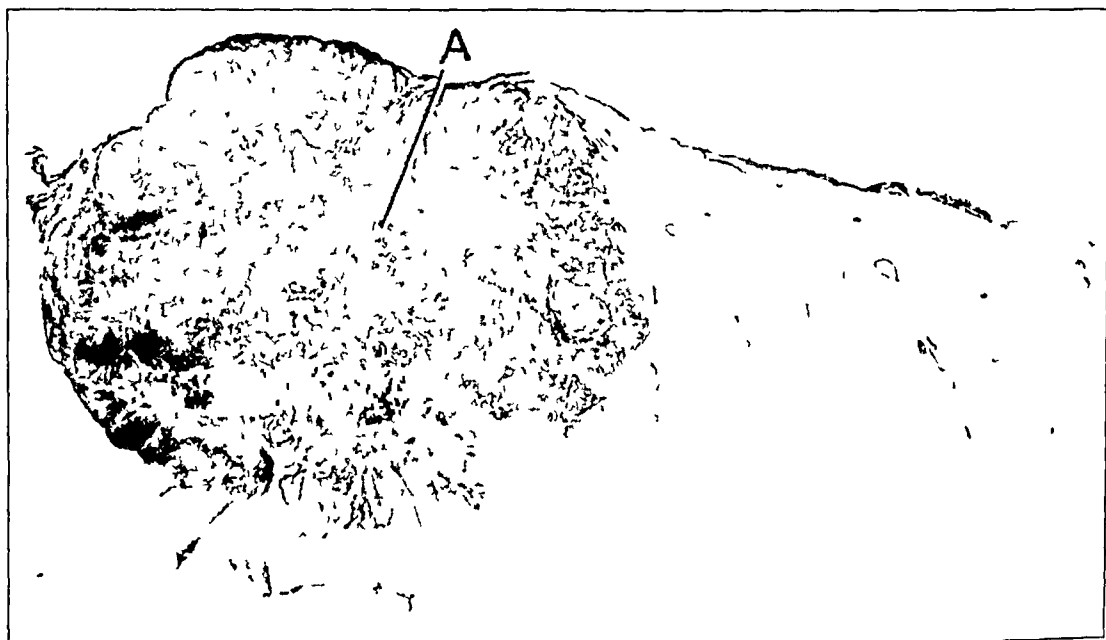


Fig 9 (case 4)—Part of a peripheral portion of a breast which contains carcinoma. The central parts have undergone necrosis. At the margins the surrounding fat is being invaded by carcinoma. Gelatinous foci are shown in figure 10.

lump about 3 cm in diameter situated at the periphery of the outer segment of the breast. The skin was adherent to it. The nipple was not retracted and there was no discharge of blood from the nipple. The right axillary lymphatic glands were hard and confluent. There were no enlarged supraclavicular glands. The opposite breast was normal.

*Pathologic Examination*—The tumor measured 2.5 cm in diameter, was situated at the periphery of the breast and was composed almost entirely of epithelial cells that had invaded the stroma and the surrounding fat of the gland (fig 9). The epithelium was highly anaplastic. Gelatinous degeneration had occurred in a small patch of the tumor that was detected only by microscopic examination.

(fig 10) Gelatinous degeneration had begun among small groups of cells adjacent to this patch (fig 10, *A*, *B* and *C*) The lymphatic glands were extensively invaded

*Comment*—This specimen is another example of a highly anaplastic and malignant tumor that contains gelatinous degeneration The carcinoma was advanced and had spread so diffusely that it had obliterated all signs of its primary site of origin Where the gelatinous

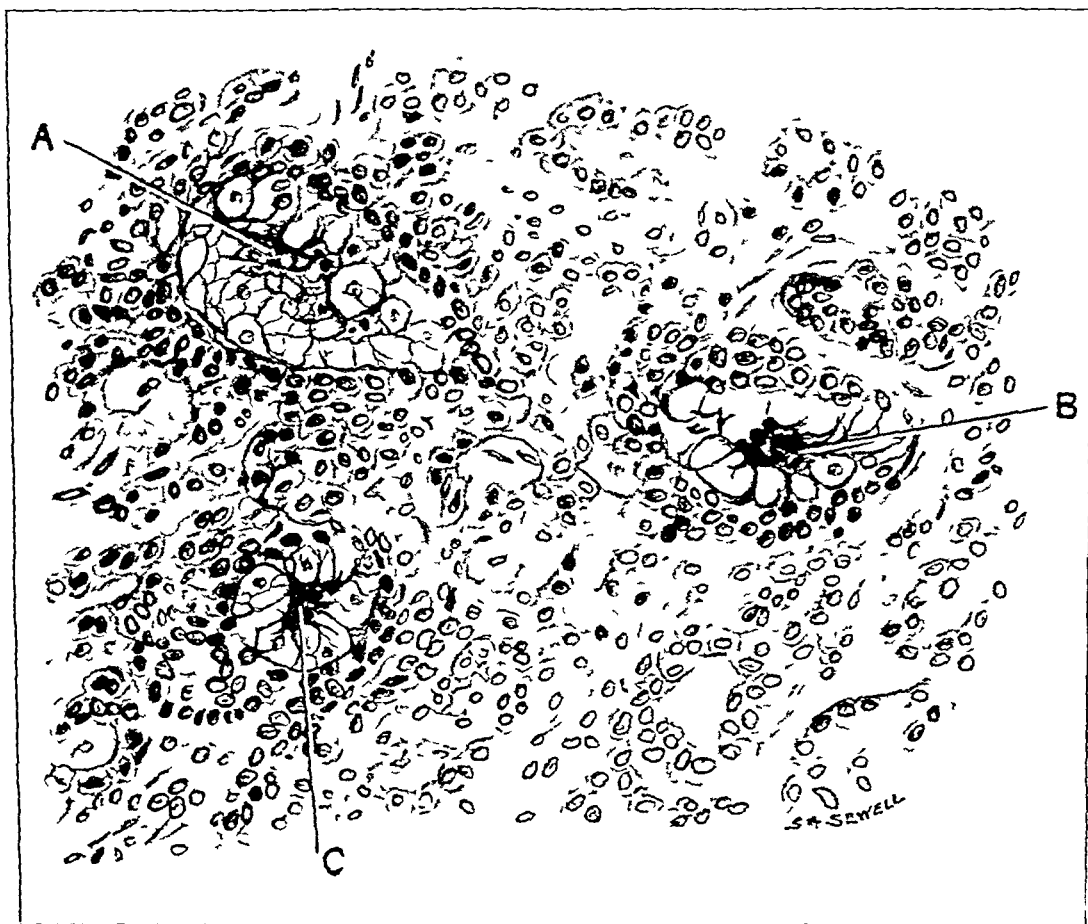


Fig 10 (case 4)—Drawing under high power of three loci of gelatinous degeneration (*A*, *B*, *C*) occurring in the center of collections of epithelial cells that have invaded outside tissues The drawing is made from the tumor shown in figure 9

degeneration could be seen in the early stages it was occurring in the epithelial cells The patient died two and one-half years after operation of pulmonary metastasis

CASE 5—A married woman aged 50 with no children two years before admission noticed a lump to the right of the left nipple from which there was a discharge of blood which soon disappeared and never recurred

*Clinical Examination*—On the right of the nipple and in immediate juxtaposition to it there was a flat, round, firm swelling with well defined margins which pushed the nipple to one side. The skin was adherent to the tumor. The remainder of the breast was normal on palpation. The complete operation was performed on the assumption that the swelling beside the nipple was a duct carcinoma and was the cause of the discharge of blood from the nipple. During the operation the lymphatic glands in the axilla were discovered to be enlarged, hard and discrete. The thick layer of fat obscured their presence and prevented them from being felt on palpation.

*Pathologic Examination*—Whole sections were cut of this breast, and the following conditions were revealed. The tumor beside the nipple was composed entirely of infiltrating carcinoma among which there was no sign of a duct. As

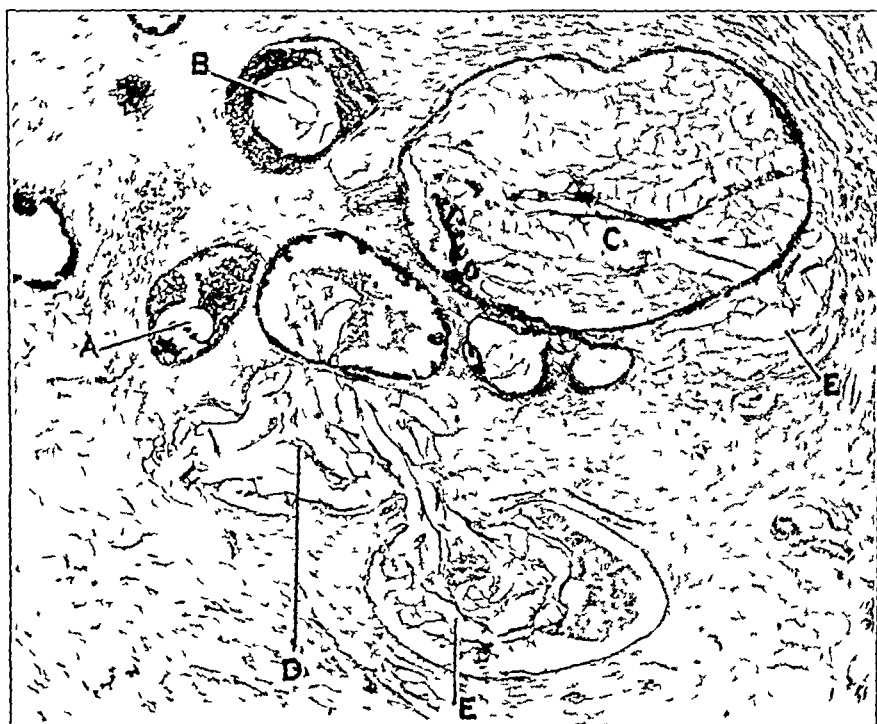


Fig 11 (case 5)—A lobule in which various stages of gelatinous degeneration are seen in different acini. *A*, acinus in which gelatinous degeneration is in an early state, *B*, acinus in which the degeneration has occurred in the center, leaving layers of unaffected epithelial cells around its margin, *C*, acinus filled with and distended by gelatinous degeneration of epithelial cells, a few of which are still to be seen within the structure, *D* and *E* acini which have become confluent and are filled by gelatinous degeneration only.

this discovery did not account for the discharge of blood from the nipple, more sections were cut in search of its cause. At the periphery of the outer middle segment of the gland carcinoma was discovered affecting a large area of terminal ducts and acini. Many terminal ducts and acini contained epithelial neoplasia within normal boundaries. In a few small scattered parts of the stroma and surrounding fat epithelial cell invasion had occurred. In the terminal ducts the epithelial neoplasia was chiefly papillomatous in type, in the acini it was sessile

only. In these parts the epithelial neoplasia looked malignant and in scattered areas had undergone gelatinous degeneration. Figure 11 shows four stages of mucoid degeneration which could be traced from its beginning to its final state. The earliest visible changes that could be detected may be seen in figure 12, which shows a terminal duct distended by epithelial neoplasia. The epithelium in this acinus contained many cells which were swollen and clearer than normal. The edges were well defined. The nuclei were smaller and appeared shrunken. A further stage of mucoid degeneration may be seen in figure 13 in an adjacent terminal duct which was distended by the same type of neoplastic epithelium. In the center of the acinus the final stages of gelatinous degeneration had been reached and several degenerated cells may be seen in the middle of the gelatinous material (fig. 13 B). The surrounding cells were in the same state as the affected cells.



Fig. 12 (case 5)—High power magnification of a terminal duct distended by epithelial neoplasia. *A* the marginal layers of epithelium show the earliest stage of gelatinous degeneration. The cells are swollen and the nuclei appear small and shrunken. *B* in the center of the duct gelatinous degeneration is marked. The elastica around this duct has undergone hyperplasia.

Figure 11 shows a group of acini in all the stages of gelatinous degeneration including its final phase. At *A* the process is in an early stage. At *B* it is more advanced and small islands of epithelial cells can be seen in the midst of gelatinous material around the margins of which are epithelial cells which have not undergone complete degeneration. At *C* there is another acinus filled with and distended by gelatinous degeneration in which islands consisting of a few degenerated epithelial cells can be seen. At *D* and *E* gelatinous degeneration has extended to such a degree that no evidence of epithelial cells can be detected and the delicate gelatinous meshwork is all that can be seen.



*Comment*—In this illuminating and interesting specimen the origin, course and final stages of gelatinous degeneration could be traced. The process began and ended in epithelial degeneration. The morphologic appearance exhibited an unbroken chain of events. The areas in which gelatinous degeneration appeared to have infiltrated the connective tissue stroma of the breast were really the remains of degenerated epithelium which had completely disappeared, leaving a gelatinous meshwork within the distended acinus. Gelatinous degeneration is not an infiltrating process and does not begin in the connective tissue, it is



Fig 13 (case 5)—High power magnification of terminal duct in which gelatinous degeneration has progressed farther than in the terminal duct in figure 12

only an epithelial degeneration. Gelatinous degeneration can also occur in epithelial cells that have invaded normal structures. This degeneration occurring in carcinoma may give rise, as in case 6, to the appearance of a gelatinous degeneration beginning in or infiltrating connective tissue.

**CASE 6—Clinical History**—A woman aged 42 married, with one child, had noticed pain in the right breast for twelve months. There was no discharge of blood from the nipple. On examination a large tumor 3 cm in diameter was found in the outer middle segment of the right breast. The nipple was movable

and not retracted. The tumor was adherent to the skin. The axillary lymphatic glands were hard, round and confluent near the breast. They were discrete and enlarged in the upper part of the axilla. The breast moved freely on the deeper structures. The whole breast was removed, and the patient died five years after the operation.

*Pathologic Examination*—Whole microscopic sections showed that the tumor was large and triangular (fig 14). The large size of the tumor was caused by the extensive epithelial invasion that had occurred in the stroma of the breast and



Fig 14 (case 6)—Whole microscopic section of breast. *A* nipple, *B* tumor, *C* pectoralis major, *D* a large duct, a high power magnification of which is shown in figure 15. The neoplastic epithelium of this duct and its acini is the only seat of gelatinous degeneration that could be detected in this breast.

the fat immediately surrounding it. In other parts malignant epithelial neoplasia could be seen distending the ducts and acini. In one of these ducts (fig 15 *A*) it had undergone extensive gelatinous degeneration and islands of degenerated epithelial cells could be seen suspended in the typical gelatinous material. Figure 15 *B* shows that the acini which communicated with this duct had also undergone epithelial neoplasia and subsequent gelatinous degeneration. There was no other evidence of gelatinous degeneration in this tumor. The epithelial ele-

ments of the tumor were highly anaplastic. The elastica had undergone a certain amount of hyperplasia throughout the whole breast.

*Comment*—This tumor has two points of interest. 1. The gelatinous degeneration was limited in extent, its presence was totally unsuspected and would probably have been missed had not whole microscopic sections of the breast been cut. 2. The epithelial elements of the tumor were highly anaplastic. The accidental discovery of the gelatinous degeneration in this tumor also suggests the probability that gelatinous degeneration may be more common than is generally supposed. The clinical history and microscopic appearances afford further evidence



Fig 15 (case 6)—High power magnification of duct (*A*) and its acini (*B*) taken from figure 14 *D*, showing large duct containing neoplastic epithelium, some of which has undergone gelatinous degeneration. Outside these structures carcinoma is rampant.

that carcinomas in which gelatinous degeneration has occurred can be highly malignant.

*CASE 7—Clinical History*—A married woman, aged 45, with two children, noticed a lump in the left breast eight months before operation, during which time it gradually increased in size. On clinical examination, a large hard, round tumor occupied the right side of the breast near the nipple. The skin was adherent to it. The nipple was movable and not retracted. The axillary lymphatic glands were not enlarged.

*Pathologic Examination*—The tumor was large and round, measuring 3 cm in diameter. To one side of and below its center was a large isolated area of gelatinous degeneration in which islands of degenerated epithelium could be seen (fig 16). Disconnected strands of connective tissue could be seen amid the

gelatinous degeneration, they showed no sign of gelatinous change. The epithelium was not highly anaplastic. At the margin of the tumor ducts could be seen containing papillomas covered by three or more layers of epithelium. Sessile epithelial growth also existed in these ducts. The arrangement of the tissues composing this tumor was in many parts papillomatous, and its site of origin was undoubtedly one of the large ducts. There was extensive epithelial invasion of the stroma, but the surrounding fat had not been invaded. The axillary lymphatic glands were not invaded by the disease.

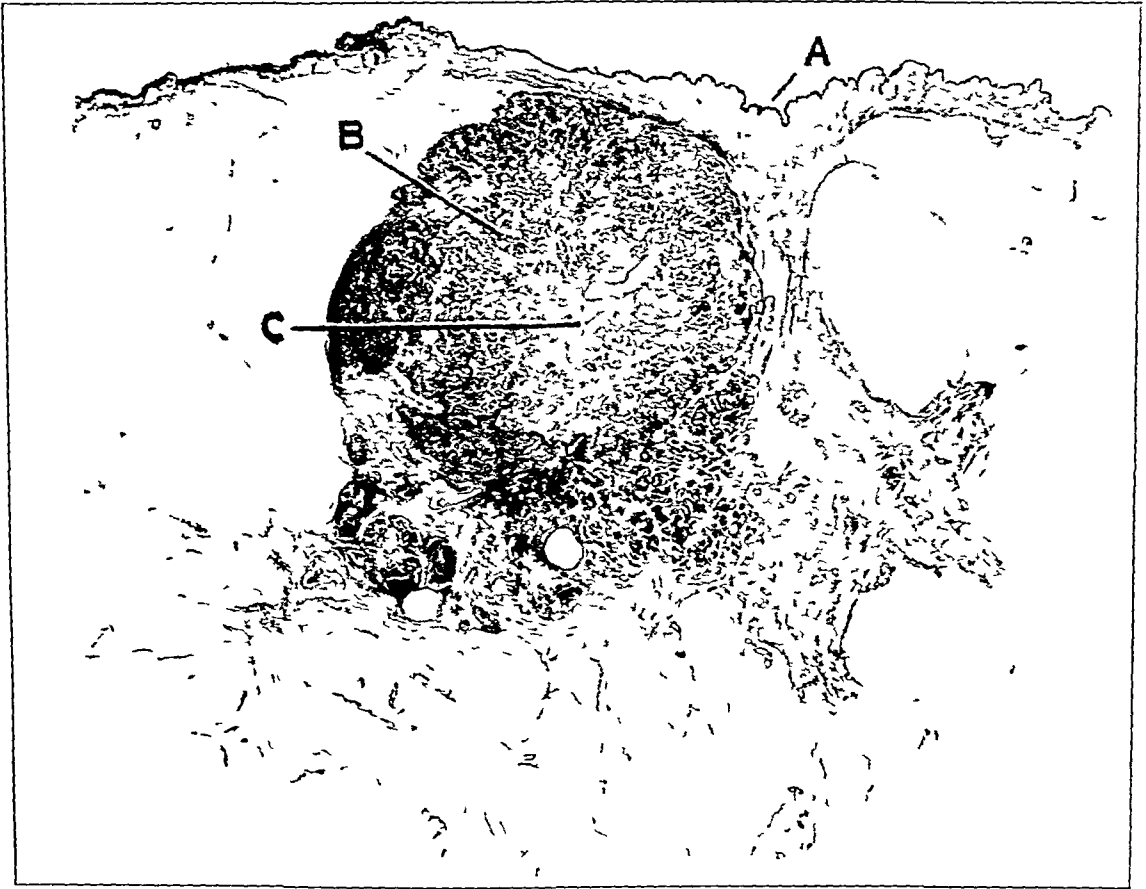


Fig 16 (case 7) —Whole microscopic section of breast. *A*, nipple, *B*, tumor, *C*, site of gelatinous degeneration. The tumor is a large duct carcinoma in the center of which (*C*) gelatinous degeneration has occurred.

*Comment*—This tumor belongs to the class in which gelatinous degeneration has occurred in a carcinoma that is not highly anaplastic. The carcinoma was not so rampant as to destroy all traces of its sites of origin in the larger ducts in spite of its large size. Its relatively

low state of malignancy was also indicated by the absence of lymphatic glandular involvement, although the tumor was a large one

**CASE 8—Clinical History**—A woman, aged 57, married, with two children, complained of an aching pain localized to the middle outer segment of the left breast, which she had noticed for five months. She had also felt a lump in the breast and had noticed a brownish intermittent discharge from the nipple for the same period. On examination she appeared thin, and the breasts were small. On palpation, a localized, comparatively extensive area of fine nodularity was discovered in the painful part of the breast. It was not adherent to the skin or to the underlying tissues. The nipple was normal, and there were no enlarged glands

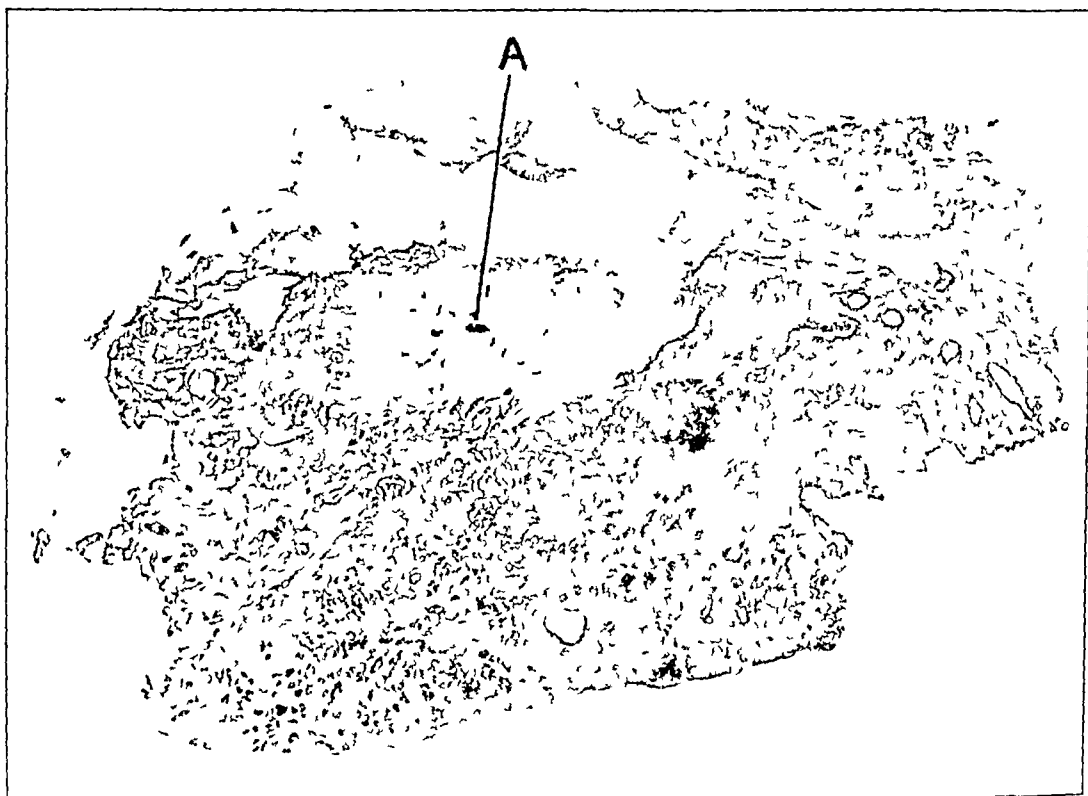


Fig 17 (case 8) —Whole microscopic section of the breast. The diseased area is triangular with the apex of the triangle directed toward the nipple. It is composed of many small cysts which are distended by neoplastic epithelium. At the base of the triangle is present the epithelium of which is undergoing gelatinous degeneration.

in the axilla. The opposite breast was normal. On the basis of these clinical signs alone radical operation was performed.

**Pathologic Examination**—Figure 17 shows a vertical section of the breast that was cut in a plane parallel with the anterior surface of the body. Many small cysts full of epithelial neoplasia were visible. These cysts were ducts and were distended by epithelial neoplasia which was not very anaplastic. Epithelial cells could be seen invading the stroma of the breast where gelatinous degeneration was marked. Here and there in the center of some of the cysts, epithelial cells

had undergone gelatinous degeneration to a slight degree (fig 18). The elastica stained normally. The lymphatic glands in the axilla were free from disease.

*Comment*—This specimen demonstrates the importance of localized nodularity in a breast as a sign of early carcinoma. This sign is important whether or not it is accompanied by pain. Case 8 is another example of gelatinous degeneration beginning in epithelial cells. It resembled cases 1, 2 and 3 in that the primary neoplastic epithelial change within the ducts and acini was extensive and largely confined within normal boundaries. The limitation of the carcinoma in the breast can probably be explained by the fact that the epithelial neoplasia was



Fig 18 (case 8)—High power view of two cysts in figure 17 showing different stages of gelatinous degeneration in the center and along the margins.

not highly anaplastic. In this specimen the gelatinous degeneration was early and slight and might easily have been missed had it not been for the fact that whole microscopic sections were cut of the breast.

#### SUMMARY AND CONCLUSIONS

The study of whole microscopic sections of carcinoma of the breast in which gelatinous degeneration had occurred has led to the following conclusions:

1. Gelatinous degeneration is more common in carcinoma of the breast than is generally supposed. This conviction is based on the fact

that from a study of whole sections we have discovered gelatinous degeneration in tumors in which its presence was totally unsuspected. These observations lead us to believe that if carcinomatous breasts were always systematically examined by means of whole serial sections, the discovery of gelatinous degeneration would be more frequent.

2 The process of gelatinous degeneration begins and ends in the epithelium only. The study of specimens that show gelatinous degeneration in all stages convinces us of this fact. Moreover, the presence of gelatinous degeneration in metastatic deposits is further evidence in favor of its origin in the epithelium.

3 The areas in which gelatinous degeneration appears to have infiltrated the connective tissue stroma of the breast consist of the remains of degenerated epithelium which has disappeared completely, leaving only a gelatinous meshwork. This gelatinous degeneration begins and ends in epithelium confined within ducts and acini and also affects the epithelium that has invaded normal structures. The final stage of both events gives rise to morphologic appearances that have been interpreted as evidence of a primary gelatinous degeneration in connective tissue cells.

4 The large size of some of the tumors we have examined has been due to the wide distribution of apparently malignant epithelial neoplasia existing in ducts and acini. Whole or chief parts of a duct or even two ducts and its terminal branches and acini may be thus affected.

5 The presence of gelatinous degeneration in a carcinoma of the breast does not necessarily imply a low degree of malignancy, as is generally supposed. Four of our cases were among the most malignant that can be encountered in the breast, and in all death resulted from the disease. Morphologically, they were highly anaplastic, and clinically their high degree of malignancy was demonstrated by prompt recurrence, widespread metastasis and a rapid course.

6 The clinical course of tumors exhibiting gelatinous degeneration is determined chiefly by the precise biologic properties of the epithelial elements they contain and does not depend on either the presence or the extent of the gelatinous degeneration.

7 Carcinomas of the breast exhibiting gelatinous degeneration often possess a comparatively low degree of malignancy. On the whole, however, we believe that gelatinous degeneration is one of the secondary and adventitious changes that may occur in the course of any carcinoma and does not necessarily determine the degree of malignancy of the tumor.

## GOITER

### MANAGEMENT OF THE POOR SURGICAL RISK\*

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Since the advent of aseptic surgery, the introduction of iodine in the preoperative preparation of patients with exophthalmic goiter has been the most momentous single advance made in the surgical treatment for diseases of the thyroid gland. Viewed either as to its revolutionary beginning or as to its far-reaching effect on the whole field of surgical treatment for the thyroid gland, the year of its discovery has opened a new era in the progress of this branch of surgery. The contrasts between the new and the old are great. In numerous articles attention has been called to the pronounced effect of the administration of iodine on the pathologic changes in the gland and on the course of the disease as evidenced particularly by the change in the symptoms and the appearance of the patient, by the lowering of the basal metabolic rate and by the absence of severe postoperative explosive reactions. This has resulted in a smoother convalescence, in a tremendous reduction in the need for ligations and operation performed in stages, and finally in a marked decrease in the operative mortality. As a consequence, surgery of the thyroid gland has been placed on a sound basis similar to that of other branches of general surgery, whereby in all but a small group of complicated cases the surgeon can confidently predict that if the operation is done expeditiously and without technical mishaps, the patient will easily endure the operation. This differs greatly from the conditions existing prior to the use of iodine, when in nearly 70 per cent of cases of exophthalmic goiter the surgeon feared the development of an unexpected postoperative reaction which was the immediate or contributory cause of death in more than 50 per cent of the fatal cases. To reduce the possibility of these reactions, ligations and operations performed in stages were resorted to at a tremendous cost in both suffering and economic waste. In only 30 per cent of the cases were conditions so favorable that the surgeon felt reasonably assured of the safety of primary subtotal thyroidectomy. Today safety has replaced the uncertainty of yesterday.

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\* From the Division of Surgery, the Mayo Clinic.

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Looking back to the period before iodine was used, the frequent employment of preliminary procedures and the not infrequent unexpected fatal reactions would indicate that there were no clearcut reliable criteria of the patient's condition by which the safety of surgical procedures could be judged accurately. Although it is true that the presence of severe hyperthyroidism veiling on a crisis of the disease, and the marked debility of the patient often resulting from long existing hyperthyroidism or from an associated disease were recognized as factors that would greatly increase the hazard of an operation, the fact remains that in most patients with moderate hyperthyroidism, many of whom were able to perform their daily work, there was no accurate guide to separate the good risk from the bad. In consequence of this inability to prejudge the individual hazard, the surgeon, appreciating the narrow margin of safety and sensing the many hidden pitfalls, wisely accepted nearly two thirds of the patients as uncertain or poor risks, and adjusted the entire surgical management on this basis. In order to protect such patients, any special needful treatment had to be administered also to a large group, many of whom did not actually require it. This was extravagant and, under certain circumstances, impracticable.

The introduction of iodine into the method of preparing the patient, under cooperative management, has wrought a complete change in these conditions, for no longer does the specter of death from an unexpected postoperative explosion continually confront the surgeon. With the remarkable decline in the mortality rate, the surgical treatment has been so altered that preliminary ligations have been practically abandoned and the two-stage procedures are employed only in exceptional instances in which indications are clearcut. However, excessive enthusiasm should not be permitted to impair the surgeon's critical faculties to the extent that he accepts all postoperative deaths, under the present management, as inevitable. Instead, he must search for their cause and prevention.

Are there today any recognizable factors in the patient's condition that influence the hazard of operation? In an attempt to answer this, a review was made of all the patients with exophthalmic goiter and of those with adenomatous goiter and hyperthyroidism who were operated on in the Mayo Clinic from Jan 1, 1925, to Dec 31, 1928, inclusive, with the idea of determining the influence on the mortality rate of age, duration of the disease and the severity of the hyperthyroidism as measured by the basal metabolic rate. Other factors, such as debility and the degree of myocardial or hepatic degeneration, which can often be detected clinically but which cannot be precisely estimated, were not considered. The simple goiter without hyperthyroidism was not included in the study, since the operative hazard in these cases is slight and the number of deaths is too small to be of any statistical value. During this

period there were 5 081 patients operated on for exophthalmic goiter and 2,171 for adenomatous goiter with hyperthyroidism. Forty-six of the former died—a mortality of 0.9 per cent—and twenty-nine of the latter died—a mortality of 1.3 per cent.

#### INFLUENCE OF THE DURATION OF HYPERTHYROIDISM AND AGE ON MORTALITY RATE

From the records of 1,477 cases of exophthalmic goiter it was not possible to obtain with any degree of accuracy the probable time of the

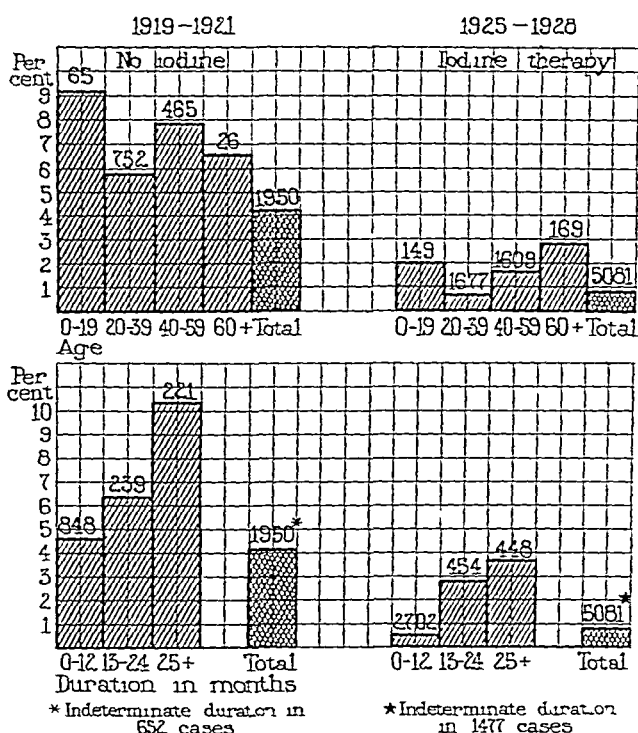


Fig 1—Exophthalmic goiter. The effect of age and of duration of disease on the mortality rate with and without iodine treatment.

onset of the disease. In the other 3,604 cases, the time of onset was definite and these were grouped under three headings, according to the duration in months of the hyperthyroidism. For comparison, a similar study was made of the records of all the patients with exophthalmic goiter operated on during the years 1919, 1920 and 1921, who had not been given iodine. Of the 1,950 patients, 81 died—a mortality of 4.15 per cent. In 1,308 cases the time of onset of the disease could be determined and they were grouped similarly according to the duration of the hyperthyroidism.

The marked benefit of giving iodine in surgical cases of exophthalmic goiter is seen by comparing the mortality rate in the two series (fig 1). In both series the duration of the disease exerted a pronounced influence on the mortality rate, more marked in the later series, in which iodine had been given. This can be explained by the fact that in the early case of exophthalmic goiter there is usually only one additional operative hazard, the severity of the hyperthyroidism, while in the late case there are two, the severity of hyperthyroidism and the presence of visceral degeneration. As iodine will largely control the danger incident to the severity of the hyperthyroidism, it has eliminated the only additional surgical hazard in the early case, whereas it has removed only one of the two hazards in the late case. It is apparent, then, that the longer the patient has the disease before submitting to surgical procedures, the

*Duration of Exophthalmic Goiter*

Year	Average Duration of Hyperthyroidism Months	Patients Having Hyperthyroidism for Twelve Months or Less Per Cent
1909	31.24	45.36
1910	33.56	40.17
1911	24.62	57.60
1915	23.37	57.61
1916	23.19	63.23
1917	19.55	68.31
1918	22.57	61.82
1919	20.26	64.07
1920	19.16	65.68
1921	19.59	63.42
1922	18.31	65.81
1923	18.02	67.20
1924	21.00	69.95
1925	21.60	69.96
1926	15.90	76.37
1927	15.40	77.94
1928	14.35	75.21

greater the operative hazard. However, there is a definite trend year by year for the patient with exophthalmic goiter to seek operation sooner after the onset of the disease (table), and this is the most hopeful sign in the solution of the goiter problem.

Among patients having adenomatous goiter with hyperthyroidism, the duration of the hyperthyroidism had an equally significant influence on the mortality rate (fig 2).

With the exception of the group of patients aged less than 20 years, the advance of years beyond 40 is an increasing factor of significance in the surgical mortality rate in cases of exophthalmic goiter. It would appear that the resistance to the disease in the young is definitely less than after full maturity. This fact has long been recognized, and for the young a longer period of preoperative preparation has been urged.

Age plays a far more prominent part in the mortality rate of patients who are suffering from adenomatous goiter with hyperthyroidism than of those who have exophthalmic goiter. One patient,

a girl aged 19 who had been an invalid for many years as the result of an attack of anterior poliomyelitis in childhood, was the only patient aged less than 20 who died. Because of great weakness she was unable after operation to raise the mucus, the mucus accumulated and she literally drowned in her own secretions; age was in no way a factor. The greatest mortality rate occurred in patients of advanced years.

#### HEIGHT OF BASAL METABOLIC RATE

In the analysis of this series of cases of exophthalmic goiter, it was clearly demonstrated that the height of the basal metabolic rate

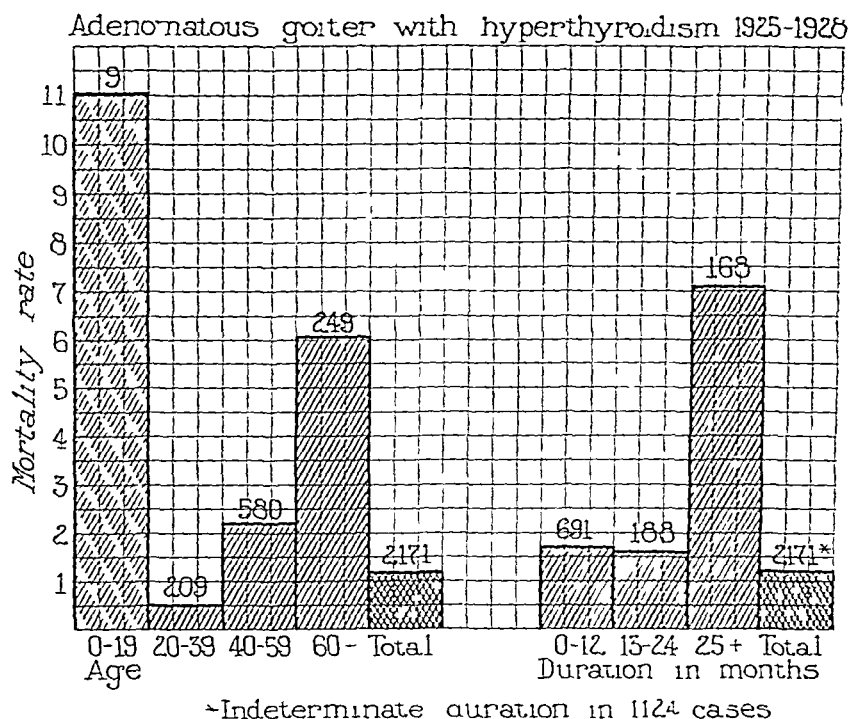


Fig 2—Adenomatous goiter with hyperthyroidism. The effect of age and of duration of the disease on the mortality rate.

was a significant factor in the mortality rate. Viewed as a whole, a considerably larger percentage of deaths occurred if the basal metabolic rate was more than  $+50$  than if it was less than  $+50$ , and it would appear that the higher the rate above  $+75$ , the greater the operative hazard (fig 3 a). Contrasting the two series of cases of exophthalmic goiter, it was found that twenty (1 per cent) of the patients who had been operated on without being given iodine died from a postoperative hyperthyroid reaction within twenty-four hours, whereas only seven (0.14 per cent) of those who had had iodine died in a similar manner.

It would seem that the effect of iodine was greatest on the patients with a moderate or low basal metabolic rate (fig 3 *b*). The influence of the height of the metabolism on the surgical hazard in the cases of adenomatous goiter with hyperthyroidism is similar to that in cases of exophthalmic goiter (fig 3 *c*).

#### SURGICAL HAZARDS

The increased potential hazards in surgery of toxic goiter can be conveniently divided into (1) the development of an overwhelming postoperative hyperthyroid crisis, (2) the debility of the patient resulting from the intensity of the disease or the long continued hyperthyroidism, advanced age, or from some intercurrent disease, and (3)

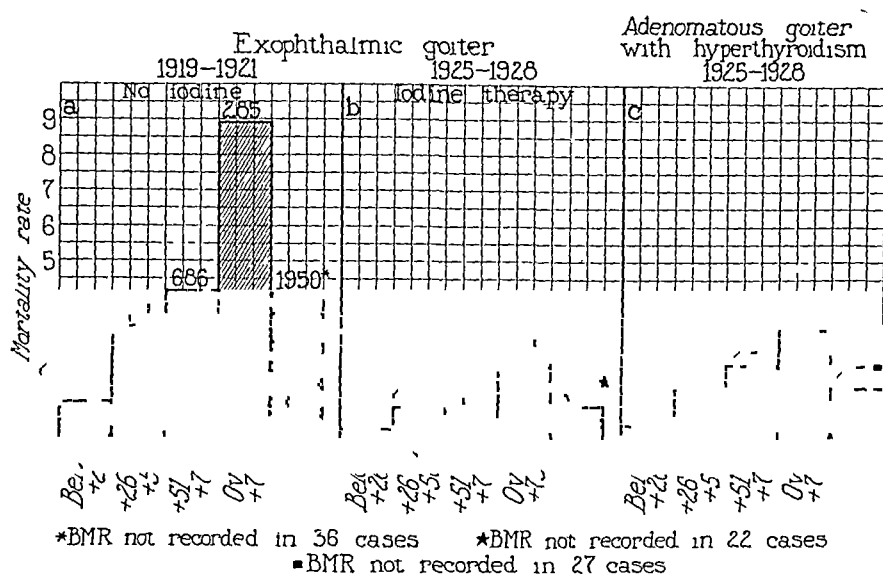


Fig 3—Mortality rate based on the height of the basal metabolic rate *a*, exophthalmic goiter without iodine treatment, *b*, exophthalmic goiter with iodine treatment, and *c*, adenomatous goiter with hyperthyroidism

increased technical difficulties occasionally met with in huge obstructive goiters. In fifty-eight of the seventy-five fatal cases in this series, necropsy was performed. The most common anatomic abnormalities were myocardial degeneration, which in five instances produced arterial emboli, pneumonia, pulmonary edema and atrophy of the liver.

Is it possible, on the basis of these potential dangers, to gage with a reasonable degree of accuracy the surgical hazard of the individual patient with goiter? To determine this a written preoperative record must be made of the individual ratings of all patients and then the mortality checked with these ratings. An attempt to carry out this plan was made on one service in the clinic. The grading of operative risks was made on the basis of 1, 2, 3 and 4. The normal risk of the

patient with goiter unassociated with hyperthyroidism was graded 1, and the normal risk of the patient with goiter associated with hyperthyroidism was graded 1+. The estimation of any additional hazard was added to the normal rating. In this series 1,486 patients with toxic goiter were operated on during the years 1927 and 1928. Eleven patients died. Of the total number, the risk in 251 cases (18 per cent) was adjudged to be moderately increased, and in fifteen cases (1 per cent)

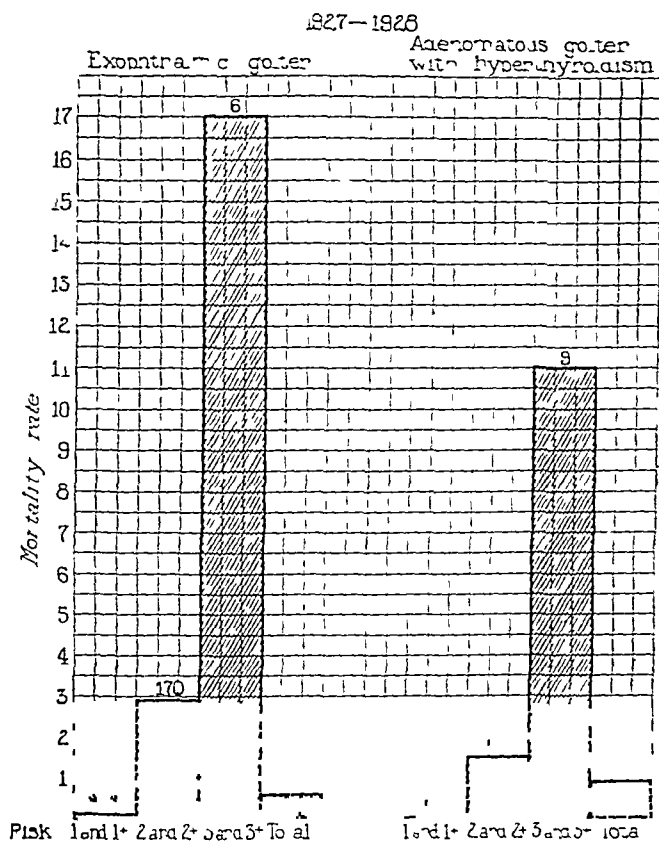


Fig 4—Mortality rate based on predeterminate risk

to be greatly increased (fig 4). Nine of the eleven patients who died were in these two groups, comprising 19 per cent of the total. It is evident that although it is not possible to foretell which patient will not survive the operation, it is possible from a clinical estimate of the hazard to select a small group (19 per cent) from which 81 per cent of the mortality will be derived.

#### TREATMENT

The treatment of the patient representing a poor risk is divided into three stages, preoperative, operative and postoperative, no one of which

can be considered to outrank the others in importance, as success is frequently dependent on the careful management of all three

*Preoperative Treatment*—Secondary in importance only to iodine treatment has been the organization of cooperative management of patients with toxic goiter whereby throughout the entire period of observation they are under the joint supervision of the internist and the surgeon. Under such a system the operative hazard can be more accurately estimated, the patient who is a poor risk can be prepared more intelligently and complications can be more quickly detected and efficiently managed. Iodine, a diet high in calories, and adequate rest are essential to the proper preparation for operation of all patients with exophthalmic goiter. The details of this management have been discussed frequently, and here I shall emphasize only certain additional measures necessary for the handicapped patient.

Not infrequently, patients with severe hyperthyroidism are operated on before they have been adequately prepared. This error is sometimes accounted for by an unfounded belief that the effect of iodine on the disease is transient, and that to obtain its maximal benefit the operation must be performed within the limited time of from two to three weeks. Although from eight to twelve days is sufficient time for the preparation of most patients, a considerably longer period is required by others, particularly those who on admission are greatly prostrated from acute severe hyperthyroidism. To operate on such patients before they have at least partially regained their weight and strength may prove disastrous, but a delay of three or four weeks or longer will insure an easy convalescence. Adequate rest does not necessarily imply continuous confinement to bed up to the time of the operation. This is debilitating, and when a patient is thus confined he becomes a fit subject for the development of postoperative pulmonary complications. If strict confinement is necessary, as it is for patients with cardiac decompensation, it is advantageous for the patient to be up and about a part of each day, until he has recovered his strength, before operation is undertaken. In my experience, the observance of this rule has been of inestimable value.

In preparing patients with obvious cardiac disease, one is frequently tempted to administer digitalis in the hope of quieting the heart and increasing its reserve. Since 1923, however, at Plummer's suggestion digitalis has been given only occasionally, for example, to patients with cardiac decompensation when rest alone has failed to restore the compensation. The results have fully justified this policy. Deaths cannot be attributed to failure to give digitalis, and unquestionably convalescence has been smoother.

Patients with degenerative changes in the liver, as evidenced by the phenoltetrachlorophthalein retention test, and those with diabetes mellitus

may have the glycogen reserve materially increased by preoperative preparation in the first group by the intravenous injection of 10 per cent dextrose in sodium chloride solution and in the second by a diet high in calories and rich in carbohydrates supplemented by adequate insulin to make possible its utilization

*Operative Treatment*—The choice and the manner of administering the anesthetic are of prime consideration in the operative treatment of the patient who is a poor risk. It is not unusual for enthusiasts to advocate some particular inhalation anesthetic as being peculiarly suitable for operations on patients with goiter. From my experience I am in thorough accord with the teachings of Crile, that the employment of prolonged inhalation anesthesia is deleterious to the handicapped patient. Local anesthesia alone is not essential, and moreover it cannot be administered successfully to many of the patients. I have found that infiltration with procaine hydrochloride supplemented by nitrous oxide and oxygen is the most satisfactory method of anesthesia. Under this method the average duration of administration of gas is from eight to ten minutes. For patients with obstructive dyspnea local anesthesia is definitely indicated. Sodium amytal (sodium iso-amylethyl barbiturate) narcosis has been employed in the Mayo Clinic with success in many operations on the thyroid gland, but I am of the opinion that it has one disadvantage which should prevent its general use in this field. Patients are asleep during the entire operative procedure, and therefore it is not possible to test the function of the vocal cords by having the patient speak or cough. The discovery of an injured nerve during the course of the operation may be of the utmost value in its ultimate success.

*Ligations*—In the period before the use of iodine, preliminary ligation of the thyroid vessels was a highly valuable and almost indispensable means of preparing for operation the patient who was a poor risk. It was used extensively, with most gratifying results. Today are there any indications for its employment? I said recently <sup>1</sup>

The benefits of polar ligation are obtained by reducing the intensity of hyperthyroidism. The group of patients who receive the greatest benefit from ligation are the same as the group in which treatment with iodine is most effective. The early case of severe hyperthyroidism, with pronounced bruit and thrill over the thyroid vessels, responds in a striking manner to ligation, but in this group iodine is even more effective. In the late cases with the hard, trained gland, iodine often apparently does not affect the course of the disease. In cases of this group in which benefit has not been derived by treatment with iodine and in which the operative risk is considered poor on account of the intensity of the hyperthyroid-

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<sup>1</sup> Pemberton, J. deJ. Exophthalmic Goiter. Indications for the Stage Operation, *Arch. Surg.* 18:735 (Feb.) 1929.



ism, ligation should be performed as a preliminary procedure. It has been my experience, however, that if treatment with iodine fails to influence the course of the disease, ligation is equally ineffective.

In the Mayo Clinic, ligations have not been employed in the last 2,000 operations for exophthalmic goiter.

The essential technical features of the operation for goiter consist in the removal, under aseptic conditions, of excessive thyroid tissue, with the preservation of sufficient gland to maintain the basal metabolism within normal limits, with the minimal loss of blood and with the least possible trauma to the contiguous structures. In operation on the patient who is a poor risk the avoidance of technical errors is of paramount importance, for the margin of safety is so narrow that any additional complications may prove to be just sufficient dead weight to tilt the scales to the disadvantage of the patient. Theoretically the list of the possible errors would make a varied and formidable array, but actually under modern methods only two occur with a degree of frequency to be worthy of special note, namely, injury of the recurrent laryngeal nerve and postoperative hemorrhage. Both of these can be prevented only by extreme care in details. If the surgeon is in the least uncertain as to the effectiveness of the hemostasis, one of two additional steps is advisable: ligation of one or both inferior thyroid arteries at a point proximal to their entrance to the gland, or packing the cavity and leaving the wound open. I frequently adopt the former procedure (fig 5). As I have previously pointed out,<sup>2</sup> the strict adherence to two principles of technic will greatly lessen the chance of injuring the nerve: the preservation of the posterior mesial portion of each lateral lobe, and the avoidance of exposure of the lateral wall of the trachea. In all cases it is highly desirable that the functional integrity of the nerve be determined by having the patient awakened and by noting the character of the voice or cough after resection of the first lobe.

In the event of injury of a nerve during the removal of the first lobe, the surgeon must be acquainted with that fact before the resection of the second lobe. Experience has proved that the immediate removal of a constricting suture unwittingly placed around the nerve will result in complete functional restoration in from six to ten weeks, on the other hand, I believe that all such sutures allowed to remain will eventually cause permanent paralysis of the nerve. If the nerve has been injured during the operation on a patient, who is a poor risk, this should be a definite indication to defer the resection of the second lobe until a later date. Likewise, if the resection of the first lobe is attended

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<sup>2</sup> Pemberton, J. deJ. Obstructive Dyspnea Following Surgery of the Thyroid Gland and Its Prevention, *S. Clin. North America* 4: 451, 1924.

by excessive loss of blood or undue prolongation of the operation, it is advisable to postpone the operation on the second lobe. Lobectomy may be indicated in another group of late cases of two years' standing or longer, in which the glands are large and firm and may be technically difficult to resect. Most such patients will safely tolerate uncomplicated

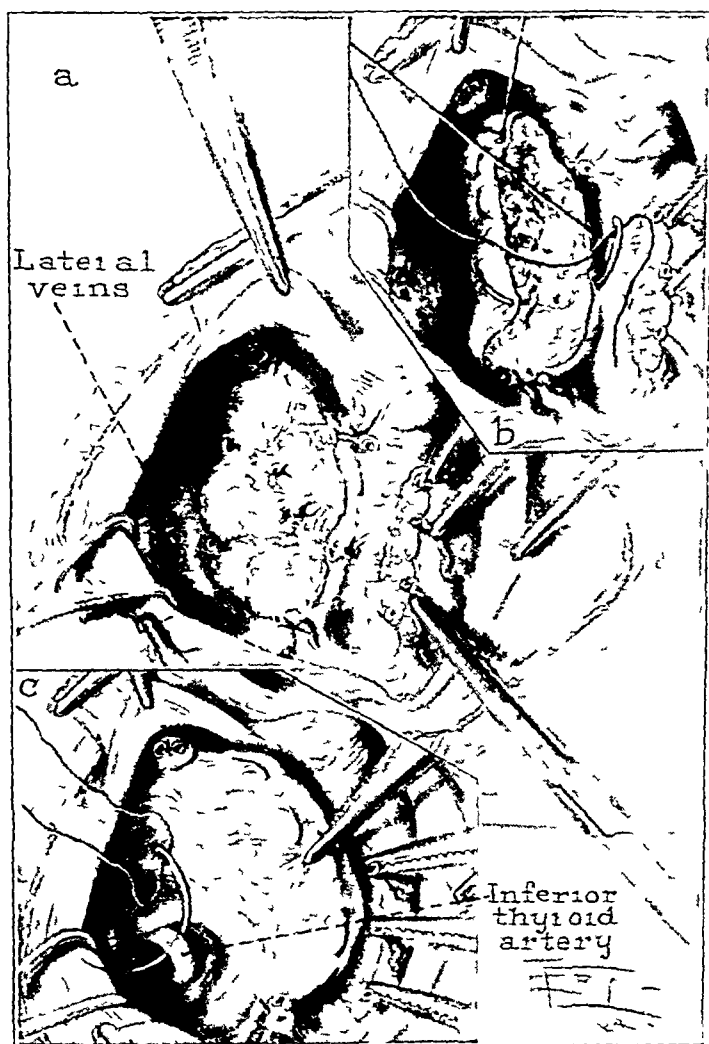


Fig 5—Methods of controlling bleeding: *a*, ligation of the branches of the individual vessels; *b*, hemostatic suture of the remnant of the gland; and *c*, ligation of the inferior thyroid artery at a point proximal to its entrance into the gland.

subtotal thyroidectomy, but would probably succumb if there were any additional burdens, such as those imposed by the occurrence of a technical error. Any modification of the operative procedure that would

improve the patient's condition at a reduced risk should be substituted for primary subtotal thyroidectomy. The operative risk of lobectomy is definitely less than that of subtotal thyroidectomy, for the surgical trauma and the chances of a technical error attendant on the former are just half those of the latter. If the patient can endure lobectomy, the resulting improvement will be so marked that the second lobe can be resected later at a greatly diminished hazard. An accident at the second stage would not necessarily prove disastrous. As a matter of record, in the Mayo Clinic, the operation in stages is now being employed in less than 1 per cent of all cases of toxic goiter.

*Postoperative Treatment*—During immediate convalescence a large percentage of the patients do not require special treatment other than the symptomatic measures employed as a routine. However, it is probable that in no other field of surgery can more be accomplished in the treatment for grave complications. As already indicated, the most frequent postoperative complications are obstructive dyspnea, acute hyperthyroid reaction, and pulmonary edema and infections, and, as successful management of these is dependent on early recognition of impending signs and the prompt institution of proper treatment, close supervision by an experienced internist is indispensable. It is for this type of complications, associated with cyanosis, that oxygen treatment, particularly in the oxygen chamber, has proved to be of great value. Recently, Haines and Boothby<sup>3</sup> reviewed the physiologic basis of oxygen treatment and analyzed the results in the treatment for complications in 126 cases following operation on the thyroid gland. They summarized their observations as follows:

We believe that the therapeutic administration of oxygen by means of the chamber or tent is most helpful in a restricted group of cases, such as postoperative pulmonary edema, bronchopneumonia and respiratory obstruction. The patients who show most marked benefit are those with evidence of anoxemia, or of impending anoxemia. Treatment should be begun as early as possible, as in many instances the progress of pulmonary edema to pneumonia probably can be averted. Treatment should be continuous, or as nearly continuous as possible, until the pathologic process is well controlled. Treatment with oxygen can be carried out more efficiently in oxygen chambers than in oxygen tents, although excellent results can be obtained in tents properly manipulated. We do not know that the life of any individual patient has been saved by oxygen treatment, however, we believe that at least an occasional patient is saved when marked lowering of the temperature and increased comfort can be secured in such a large series of patients who are seriously ill. Our results not only warrant the continuation of this method of treatment but indicate the advisability of more general adoption of efficient methods of the administration of oxygen in those diseases

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3 Haines, S. F., and Boothby, W. M. Oxygen Treatment with Special Reference to Treatment of Complications Incident to Goiter, *Am J Surg* 7 174, 1929.

known to be benefited by its use. The patients who obtain the greatest benefit are those with postoperative pulmonary edema, bronchopneumonia, or respiratory obstruction accompanied by cyanosis or impending cyanosis.

#### SUMMARY

By contrasting the records of a large series of patients with exophthalmic goiter who were operated on after having taken iodine with a similar series of patients operated on without having taken iodine, the effect of iodine treatment was determined. The practical elimination of the need for preliminary ligations and the remarkable decrease in the mortality rate from 41 to 0.9 per cent are outstanding. Furthermore, by greatly reducing the incidence and severity of the postoperative reactions, the most uncertain of the operative hazards iodine medication has made it possible to evaluate more accurately other factors that influence the surgical mortality rate. The duration and severity of the hyperthyroidism as measured by the height of the basal metabolic rate and the age of the patient, were proved to be significant influences in the surgical hazard of all patients with toxic goiter. Other obvious factors that affect the mortality rate unfavorably are visceral degeneration and intercurrent diseases. By proper evaluation of these potential dangers, the surgeon is today enabled to predetermine with a reasonable degree of accuracy the surgical hazard of the individual patient with goiter. By means of this ability to measure the hazard it is possible to estimate the small group of patients from which the mortality is likely to be derived, and to limit the application of any additional measures of treatment needed by the handicapped patient.

The success of the operative treatment of the patient who is a poor risk is largely dependent on the avoidance of prolonged general anesthesia and of technical errors. The indications for the employment of ligation and lobectomy are limited.

Close supervision is the watchword of the postoperative care of the handicapped patient, for much can be accomplished if complications are detected early and treated intelligently. Treatment by oxygen in the chamber or tent, if instituted early, is a valuable measure in postoperative pulmonary edema, pneumonia and respiratory obstruction.

#### ABSTRACT OF DISCUSSION

DR. W. I. TERRY, San Francisco. To any one who is interested in goiter surgery this paper has been of great value. I agree with Dr. Pemberton that the use of compound solution of iodine has revolutionized the treatment for exophthalmic goiter. I cannot agree with him entirely as to its use in toxic adenomas. I have not obtained any results from using it either preoperatively or postoperatively and I discontinued using it in those cases. But with the case of hyperplastic thyroid the true exophthalmic goiter it has reduced the mortality tremendously. In the hands of any one who performs a fair number of operations for goiter the mortality from exophthalmic goiter should not be much

more than 1 per cent That is what we have had at our clinic since compound solution of iodine has been used Previously, it was 35, and even 4, per cent It was much higher than that at the hands of surgeons who were operating only occasionally for goiter Dr Pemberton did not have an opportunity to speak about the use of digitalis, but I know his views on the subject and they accord entirely with ours We use digitalis only when there is decompensation of the heart, otherwise not many of these instances of decompensation are among the cases of toxic adenoma In operating, it is important to preserve the lateral as well as the posterior capsule of the thyroid, with the object of conserving the parathyroids and the recurrent laryngeal nerve This technic has been described by us elsewhere

DR THOMAS M JOYCE, Portland, Ore Symptoms and physical signs referred to the heart are sought for and expected to be found in every case of thyrotoxicosis in which other clinical symptoms of thyroid hyperplasia are met These symptoms vary from simple tachycardia to signs of well marked congestive cardiac failure We have not recognized a line of demarcation between the early signs of cardiovascular disease and the late signs with which comes true failure The pathology of the heart lesion in thyrotoxicosis may not be an accepted entity, it may not be specific, although certain studies suggest a specificity

With the presence of a widespread edema, our method of treatment begins with a Karell milk diet, after two days, the diet is changed to a low protein, and salt diet and the liquid intake is restricted to 800 cc per day The Minnesota-grown powdered digitalis is administered, 4 grams (0.026 Gm) per day, until physiologic tolerance is reached All digitalis is stopped for a period of three days before operation

Sugar in the urine is a rather frequent complication of hyperthyroidism When it is due to diabetes mellitus it is a serious complication and requires careful preparation of the patient for operation On the other hand, when it can be classed as a so-called glycosuria it is of no consequence and may be disregarded When dextrose is found in the urine of a patient suffering with hyperthyroidism, a fasting blood sugar estimation should be made If the blood sugar during fasting proves to be within normal limits (between 80 and 120), this does not necessarily rule out diabetes, as many patients with mild diabetes present normal blood sugar while fasting The usual interpretation of the blood sugar curve is as follows If the blood sugar is above 160 mg in one hour and fails to return to normal an hour later after dextrose has been given, a diagnosis of diabetes can logically be made Parathyroid preservation is of great moment

Tetany is also produced by temporary swelling of the gland, shutting off of the blood supply to the parathyroids and by calcium deficiency from persistent vomiting, loss of hydrochloric acid in the stomach and consequent alkalosis Tetany is easily recognized and almost immediately relieved by the intravenous injection of parathormone and calcium chloride

Bilateral injury to the recurrent laryngeal nerve is the most serious accident that can occur in surgical measures on the thyroid Suturing of the nerves has not proved satisfactory, and the prospect of wearing a tracheotomy tube for life presents a most gloomy outlook for the patient

DR C C TIFFIN, Seattle Dr Pemberton stated that there are facing two grave dangers in thyroid surgery—hemorrhage, and injury to the recurrent laryngeal nerve The exclusive use of local anesthesia in operations on the thyroid during a period of years has caused me to give special consideration to its many

advantages The surgeon must be willing to do a little more work, but its use will minimize the dangers or injury to the recurrent laryngeal nerve During the operation, the patient is required to talk, through the continued use of the pinching forceps preceding the use of the knife, injury to the nerve is minimized This technic makes goiter surgery much safer The patient will not die of "collapsed trachea," and he can speak aloud when he leaves the operating room

The dangers of hemorrhage are minimized through the cooperation of a conscious patient I believe that thyroid surgery, done in this way, is much less of a major procedure when it is based on the great principles of careful preparation brought to our attention by Dr Plummer and the Mayo Clinic

DR E O HOUDE, Tacoma, Wash It is singular that so little distinction is made in the literature between thyroid normalcy and pathology In discussions, both are usually mixed in a maze of sophistries and paradoxes, revolving about a fetish consideration of iodine Normalcy implies a unit of measure against which pathology is weighed Acceptance of the present calculations found in literature relating to the quasistatification of the iodine deficiency theory is a tacit admission that a critical study had not been made Physiology has never contributed a direct answer to the cause of any pathology In the light of normal calculations by Kendall which show that from 1 to 2 mg of iodine per year maintains normal thyroid biologic chemistry, McClendon's normal figures in a three-day test in Minnesota which showed a calculated yearly retention of 3.65 mg from an intake of 7.3 mg, and von Fellenberg's tests on himself which showed that he eliminated the entire intake while on the low diet of approximately 0.01 mg per day, or 3.65 mg per year, the theory is built on a weak foundation, since it is shown by accepted figures that the yearly excretion, through the kidneys alone, by persons with goiter who live in the dense goiter belts is in amount not only far beyond the physiologic requirement, but in many instances is that contained in a rich hypothyroid diet

There have been no reported determinations made in any district to show a physiologic deficiency of iodine Marine states that there is yet an ultimate undetermined factor with which the peccancy of the goitrous gland must be connected

Available statistics show that only an excessive intake of iodine reduces the incidence of the disease

Bacteriology holds the key to the solution of goiter On the observations in a consecutive series of more than 500 specimens collected in the Puget Sound district, it is stated that endemic goiter is caused by a facultative anaerobic coccus, which fails to be identified with classified bacteria

The good accomplished by iodine, which invariably is given in massive doses when compared with physiologic needs, is unquestionably due to an alterative effect on the ultimate cause, whereas its occasional evil effects in the precipitation of toxic symptoms are due to a consequentially improved functional capacity of the multiplied cells, and an obviously increased thyroid secretion

The toxic types of goiter are due to and synchronous with an active infectious process which is centralized in the thyroid, by selective action, but not limited to it, its metastatic dissemination being the basis of secondary organic pathology in other parts Antigen made from cultures is specific for the infection causing endemic goiter Preoperative detoxication is effected without therapeutic administration of iodine, and postoperative autogenous antigen effects an early and complete dissipation of residual symptoms Surgery is a necessary factor in the established and irreversibly fixed goiters, but subtotal thyroidectomy with antigen treatment is a needless sacrifice of important tissues

DR J EARL ELSE, Portland, Ore Many patients with goiter cannot take compound solution of iodine They vomit It cannot be given by rectum, because it is purging Dextrose given intravenously will stop this crisis almost immediately because it is due to acidosis The toxic goiter in pregnancy causes a great deal of anxiety Some observers advise that the uterus be emptied In my judgment, there is never any indication to induce an abortion in these cases In the early months of pregnancy, with the proper treatment for the goiter the majority of patients can be operated on and go to term, without a miscarriage In the later months of pregnancy, we advise the use of roentgen rays, it is the only instance when we use the roentgen rays in the treatment for goiter With the use of roentgen rays these patients can be cared for through confinement and be operated on about six weeks later

We have had two deaths from tracheal collapse I do not believe that we should have them, we consider it our fault In the very large, diffuse adenomatous goiters, pressure on the trachea results in a weakening of the tracheal rings, so that they will collapse if the entire thyroid is removed at once When we see these cases now, and we do not see them often, we remove only one side of the gland, wait from six weeks to two months and then remove the other side In one patient whom I saw, after removing the second lobe a tracheal collapse occurred as a result of removing the entire goiter at one time, we therefore adopted the stage operation It is about the only instance in which we find an indication for stage operation I am under the impression that tracheal collapse can be prevented It must be remembered that one operates not merely to remove the goiter at the time, but to make the patient well thereafter In experimental work on animals, we found that regeneration of the thyroid was normally completed in a period of from three to four weeks, if the dogs were given iodine after the operation If iodine was not given, sometimes the hyperplasia became excessive Iodine should be given, therefore, during the regenerative period after the operation

DR J DEJ PEMBERTON, Rochester, Minn I am in thorough accord with everything that Dr King said

# THORACIC SYMPATHETIC CARDIAC NERVES IN MAN

## THEIR RELATION TO CERVICAL SYMPATHETIC GANGLIONECTOMY\*

ALBERT KUNTZ, PH D, M D

AND

ALBERT MOREHOUSE, A B

ST LOUIS

The application of surgery involving extirpation of the inferior cervical sympathetic ganglions, particularly in the treatment of patients with diseases involving the blood vessels of the upper extremities, has revived interest in the anatomic relationships of the sympathetic cardiac nerves and necessitated a reinvestigation of the exact sources and distribution of these nerves

Although Valentin<sup>1</sup> described nerves that arise from the medial aspect of the second thoracic sympathetic ganglion in man, extend medianward and downward, and send some fibers into the cardiac plexus, the more recent accounts of the innervation of the heart in man and in lower mammals, with few exceptions make no mention of cardiac nerves arising from the sympathetic trunks below the inferior cervical ganglion. According to the current textbook statements, the sympathetic innervation of the heart is mediated solely through the superior, middle and inferior sympathetic cardiac nerves, which arise from the superior, middle and inferior cervical sympathetic ganglions respectively. On the basis of this teaching it has been regarded by some as unsafe to extirpate the inferior cervical sympathetic ganglion bilaterally, since this procedure would interrupt all cardiac accelerator fibers.

The existence of cardiac accelerator nerves arising from thoracic segments of the sympathetic trunks is indicated by both clinical and experimental data. Thoracic cardiac nerves also have recently been described in man and in lower mammals. Perman<sup>2</sup> traced nerves arising from the third to the sixth thoracic ganglions into the cardiac plexus in certain *Artiodactyla* (the calf and the lamb). He was also able, in a few instances, to trace nerves from the second thoracic sympathetic ganglion to the heart in man but concluded that no cardiac nerves arise from the sympathetic trunk in man below the second thoracic segment.

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\* Submitted for publication, Oct 20 1929

\* From the St Louis University School of Medicine

1 Valentin. *Traité de neurologie* Paris 1843

2 Perman E. Anatomische Untersuchungen über die Herznerven bei den höheren Säugetieren und beim Menschen, *Ztschr f Anat u Entw* 71 382 1924



Cannon, Lewis and Britton<sup>3</sup> were able to trace nerves from the medial aspects of the first three or four ganglions below the stellate ganglion on both sides in nearly all of the cats that they examined. Occasionally they could also trace nerves medianward from the fifth and sixth thoracic ganglions. They succeeded only poorly in tracing any of these nerves to the heart, but the physiologic evidence of the existence of thoracic cardiac nerves that they obtained is convincing. Dresbach and Waddell<sup>4</sup> claimed to have traced nerves from the sympathetic trunk as low as the fifth thoracic segment into the cardiac plexus in the cat. Reigle,<sup>5</sup> who studied the innervation of the heart in apes, described rami that arise from the sympathetic trunk in the upper three thoracic segments and unite to form a single nerve that joins the middle cervical sympathetic cardiac nerve on the left and the vagus on the right side. He also described a cardiac nerve arising from the fourth thoracic sympathetic ganglion on both sides. According to Jonesco and Enachescu,<sup>6</sup> who described thoracic sympathetic cardiac nerves in the cat, dog, calf, sheep and man, these nerves are best developed in *Artiodactyla* and man. On the basis of their observations in human fetuses and two adult cadavers, they concluded that the thoracic cardiac nerves are constant in man and usually occur bilaterally. According to their observations, these nerves arise mainly from the ganglions or intervening portions of the sympathetic trunk in the second to the fifth thoracic segments. They commonly anastomose with each other and with the inferior cervical sympathetic cardiac nerve and cardiac branches of the vagus.

Our study of the thoracic sympathetic cardiac nerves in man is based on adult and young cadavers and on stillborn fetuses. The following description of the nerves is based mainly on our observations on adult cadavers. The cardiac plexuses and the intercommunications of the nerves entering them remain relatively simple in the fetus. It is possible, therefore, to trace individual nerves and their branches nearer to their terminations in relation to the heart than in the adult, but the smaller nerves entering the cardiac plexus are so delicate in the fetus

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3 Cannon, W. B., Lewis, J. T., and Britton, S. W. A Lasting Preparation of the Denervated Heart for Detecting Internal Secretion, with Evidence for Accessory Accelerator Fibers from the Thoracic Sympathetic Chain, *Am J Physiol* **77** 326, 1926.

4 Dresbach, M., and Waddell, K. C. K-Strophanthidin Emesis in Cats with Denervated Hearts, *J Pharmacol & Exper Therap* **27** 9, 1926.

5 Reigle, L. Ueber die Innervation der Hals- und Brustorgane bei einem Affen, *Ztschr f Anat u Entw* **80** 777, 1926.

6 Jonesco, D., and Enachescu, M. Untersuchungen bei Säugetieren und beim Menschen über die aus dem Brustgrenzstrang Unterhalb des Ganglion stellatum entspringenden Herznerven, *Ztschr f d ges Anat* **85** 476, 1928.

that they can be traced only with the greatest difficulty. We have therefore, preferred to describe the thoracic cardiac nerves in the adult cadaver, although it is impossible by dissection to determine the exact distribution of any given nerve within the cardiac plexus.

In all the cadavers examined a nerve could be traced from the medial aspect of both the second and the third ganglion of the sympathetic trunk below the inferior cervical ganglion or from the interganglionic portions of the sympathetic trunk in the second and third thoracic

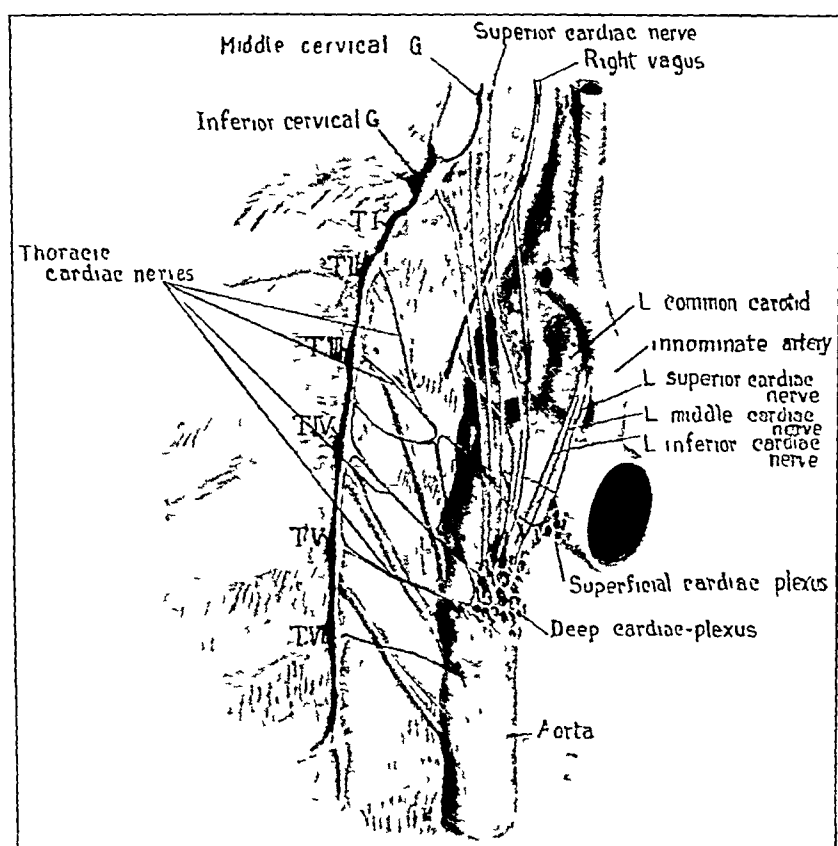


Fig 1—A drawing from a dissection of a human cadaver illustrating the nerves entering the cardiac plexus from the right side

segments. These nerves commonly unite forming a single trunk which tends medianward and downward and gives rise to branches some of which join one or more of the cervical sympathetic cardiac nerves and cardiac branches of the vagi others enter the deep cardiac plexus directly. In some instances a branch could also be traced into the superficial cardiac plexus. This branch occasionally joins the superior cardiac nerve on the left side. In many instances a ramus arising from the fourth thoracic ganglion also joins this nerve. On the right side

it passes posterior to the esophagus and approaches the deep cardiac plexus between the esophagus and the lateral aspect of the aorta. It also sends a few small branches into the right pulmonary plexus. On the left side, it passes posterior to the aorta and approaches the deep cardiac plexus from the right side. One or more branches of this nerve often anastomose with branches of the corresponding nerve on the right side before the latter joins the cardiac plexus. A nerve also arises from the fourth thoracic ganglion of the sympathetic trunk which, on the right side, can be traced directly into the deep cardiac plexus. On the left side, the nerve passes posterior to the aorta and joins the deep cardiac plexus from the right side. These nerves also supply slender branches to the pulmonary and esophageal plexuses, particularly on the right side. In the majority of the cadavers examined, slender nerves could also be traced from the fifth and sixth thoracic ganglions of the sympathetic trunk toward the aorta bilaterally. In some instances, branches of the nerve arising from the fifth thoracic ganglion on the right side could be traced into the deep cardiac plexus. Other branches became incorporated in the plexus on the descending aorta. In no case could branches of nerves arising from the sympathetic trunk below the fifth thoracic ganglion be traced into the cardiac plexus. The possibility that components of the nerves arising from the fifth and sixth thoracic ganglions of the sympathetic trunks may reach the deep cardiac plexus on the descending aorta, however, is not precluded.

Clinical and experimental data strongly suggest that the cardiac nerves that arise from ganglions of the sympathetic trunk below the inferior cervical ganglion, like the one arising from the latter ganglion, convey both sympathetic and visceral afferent fibers. The sympathetic components of these nerves are at least in part cardiac accelerators. Cannon, Lewis and Britton<sup>3</sup> were able to elicit reflex cardiac acceleration in the cat, following bilateral extirpation of the inferior cervical and first thoracic ganglions and exclusion of all humoral cardiac accelerators, until the upper six or seven thoracic segments were removed on both sides. Bilateral extirpation of the upper three or four thoracic segments of the sympathetic trunk, following removal of the inferior cervical sympathetic ganglions, in their experiments did not completely abolish reflex cardiac acceleration. Adson and Brown<sup>7</sup> also reported reflex cardiac acceleration in patients following bilateral extirpation of the inferior cervical and the first and second thoracic ganglions.

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7 Adson, A. W., and Brown, G. E. Successful Surgical Treatment of a Case of Raynaud's Disease of the Upper Extremities by Dorsal Ganglionectomy. *Proc. Staff Meet., Mayo Clin.* 3: 266, 1928.

According to Jonesco Enachescu and Teitel<sup>8</sup> stimulation of the peripheral ends of the thoracic cardiac nerves following section elicits acceleration of the heart rate and augmentation of the force of cardiac contraction. Stimulation of the central ends of these nerves elicits vascular reflexes, changes in the cardiac rhythm and pain. Mechanical and chemical stimulation of the heart and aorta in their experiments,

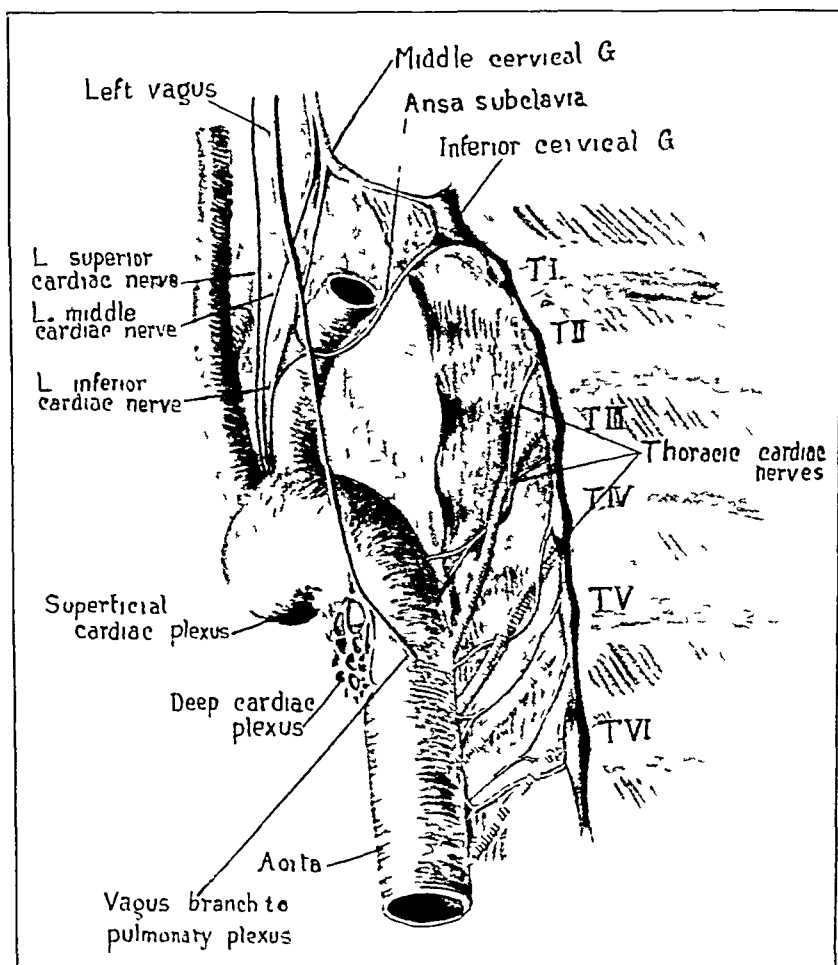


Fig 2—A drawing from a dissection of a human cadaver illustrating nerves entering the cardiac plexus from the left side

resulted in pain reactions following section of all the afferent fibers that pass through the inferior cervical and first thoracic ganglions. The same stimulation did not elicit pain reactions following section of

<sup>8</sup> Jonesco D. Enachescu M. and Teitel A. B. Ueber eine neue Gruppe von Sympathischen aus dem Brustgerenz-trang Unterhalb des Ganglion stellatum ent-springenden Herznerven. Klin. Wchnschr. 7:991. 1928

thoracic cardiac nerves in addition to bilateral extirpation of the inferior cervical and the first thoracic sympathetic ganglions

The thoracic cardiac nerves are made up mainly of postganglionic fibers that arise from neurons in the ganglions of the sympathetic trunk. The existence of medullated fibers comparable in caliber to the visceral afferent components of the inferior cervical sympathetic cardiac nerve corroborates the experimental data cited which indicate that the thoracic cardiac nerves also convey afferent impulses from the heart.

Osmic acid preparations of the thoracic cardiac nerves obtained at autopsy in a child 8 months of age show that these nerves are made

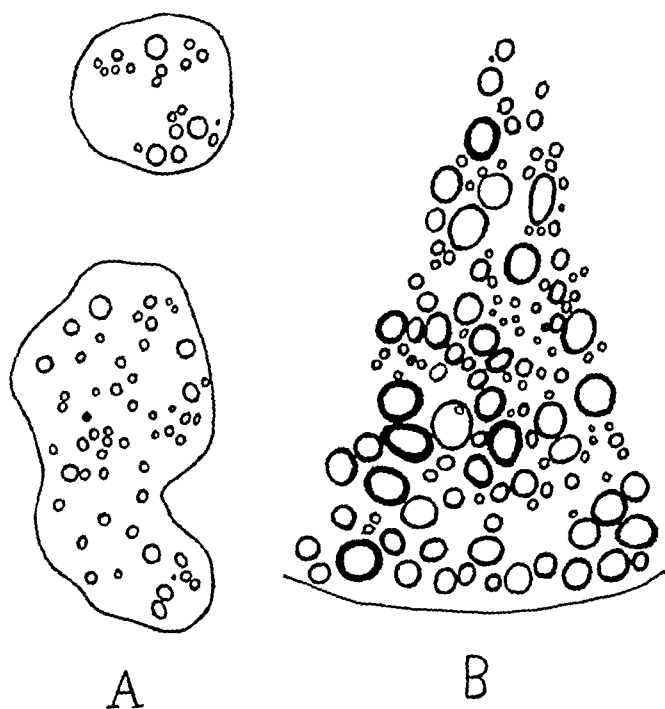


Fig 3—Camera lucida drawings of cross-sections of osmic acid preparations of nerves, illustrating distribution and relative size of myelinated fibers. *A*, thoracic cardiac nerves, *B*, sector of the dorsal root of third thoracic spinal nerve.

up mainly of unmyelinated fibers. They also contain myelinated fibers, some of which are equal in caliber to the largest myelinated fibers in the cardiac nerve that arises from the inferior cervical sympathetic ganglion. The larger fibers, doubtless, are general visceral afferent fibers supplying the heart.

Figure 3 represents camera lucida drawings of equal magnification of the myelinated fibers in cross-sections of thoracic cardiac nerves and a sector of the dorsal root of one of the corresponding spinal nerves in a dog. The thoracic cardiac nerves, as illustrated in figure 3*A*, con-

tain myelinated fibers of small and medium caliber. The smaller myelinated fibers in these nerves, like the unmyelinated fibers in them, probably are sympathetic. The larger myelinated fibers are definitely larger than the smallest myelinated fibers in the dorsal roots of the corresponding spinal nerves (fig. 3*B*). Since the preganglionic fibers involved in the innervation of the heart do not extend beyond the sympathetic trunk, and since myelinated postganglionic fibers are mainly fibers of small caliber, the larger myelinated fibers in the thoracic nerves, like the corresponding fibers in the inferior cervical sympathetic cardiac nerves, probably must be regarded as general visceral afferent fibers.

From our observations, it may be assumed that a certain percentage of both the cardiac accelerator fibers and the general visceral afferent components of the cardiac nerves remain intact following bilateral extirpation of the inferior cervical sympathetic ganglion or extirpation of this ganglion together with the first and second thoracic segments of the sympathetic trunk. More complete knowledge of the effect of extirpation of the inferior cervical sympathetic ganglions or section of the cervical sympathetic cardiac nerves on cardiac function awaits further investigation.

# NEUROPATHIES OF THE BONES AND JOINTS

## REPORT OF A CASE OF AN ARTHROPATHY OF THE ANKLE DUE TO A PERIPHERAL NERVE LESION<sup>\*</sup>

A R SHANDS, JR, M D  
DURHAM, N C

A review of the literature has revealed no complete classification of the neuropathic lesions of the bones and joints. Turney<sup>1</sup> has given the most detailed account of these abnormalities. Chipault,<sup>2</sup> Goodhart,<sup>3</sup> Albee<sup>4</sup> and others have mentioned the different conditions in which the lesions occur, but there is no agreement as to the etiologic grouping. Hence the following classification, based on etiologic factors, is presented.

- 1 Tabes Dorsalis
- 2 Syringomyelia
- 3 Following Lesions of the Peripheral Nerves
  - (a) Injury
  - (b) Peripheral neuritis
  - (c) Leprosy
- 4 Following Lesions of the Spinal Cord
  - (a) Injury
  - (b) Congenital malformations
  - (c) Tumors
  - (d) Tuberculosis of the spine
  - (e) Acute myelitis
  - (f) Anterior poliomyelitis
  - (g) Progressive (central) muscular atrophy
    - (1) Aran-Duchenne type
    - (2) Spastic type (amyotrophic lateral sclerosis)
- 5 Following Lesions of the Cerebrum
  - (a) Dementia paralytica
  - (b) Hemiplegia following cerebral hemorrhage

The first two groups, tabes dorsalis and syringomyelia, are so common compared with the others that they are given separate headings. These might be included under lesions of the spinal cord.

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<sup>\*</sup> Submitted for publication, Oct 9, 1929.

From the Orthopedic Department of the Emergency Hospital, Washington, D C

1 Turney, H C. Neurotrophic Affections of Bones and Joints, in Allbutt Clifford, and Rolleston, Humphry Davy. System of Medicine, New York, The Macmillan Company, 1910, vol 7.

2 Chipault, A. L'état actuel de la chirurgie nerveuse, 1 142, 1902.

3 Goodhart, S Philip. Vasomotor and Trophic Neuroses, in Tice, Frederick. Practice of Medicine, Hagerstown, Md, W F Prior Company, Inc, 1920.

4 Albee, F H. Orthopedic and Reconstruction Surgery, Philadelphia, W B Saunders Company, 1921.

Charcot<sup>5</sup> was the first to describe the arthropathies associated with tabes dorsalis. He presented four cases in which there appeared suddenly a firm painless swelling that extended to the surrounding soft parts and in which there apparently was no preceding trauma. The rapid changes which occurred in the surfaces of the joints gave rise to luxations and false positions of the bones shortly after the onset. Because of this early accurate description of these arthropathies, these conditions, whether associated with tabes or not, have often taken the name of Charcot joints. Allbutt<sup>6</sup> was the first to describe this condition in English, being followed shortly by Buzzard<sup>7</sup> and Thompson<sup>8</sup>.

Schultze and Kahler<sup>9</sup> (1888) were the first to describe the changes of the joints in syringomyelia similar to those found by Charcot in tabes. Schlesinger<sup>10</sup> who has collected and reported 150 cases, has given the most complete account of these joints in syringomyelia. He has shown that whereas in tabes the lower extremity is more often affected, in syringomyelia it is the upper extremity.

The first instance of changes in the joints following injury to the peripheral nerves was reported by Packard,<sup>11</sup> arthropathies of the foot and the knee followed compression of the sciatic nerve by a tumor. Weir Mitchell<sup>12</sup> reported a case in which, following an injury to the brachial plexus due to a dislocation of the shoulder, extensive joint lesions developed. He added further that wounds or any lesions of nerves may produce in the joints inflammatory conditions, usually subacute, which so precisely resemble rheumatic arthritis in their symptoms and results that no clinical skill can discriminate between the two. Mitchell<sup>13</sup> gave the first description of the spontaneous fractures which sometimes occur in tabes dorsalis. Chipault<sup>14</sup> found a destructive

5 Charcot, J. M. Sur quelques arthropathies qui paraissent dépendre d'une lésion du cerveau ou de la moelle épinière, *Arch. de physiol. norm. et path.* **1** 161, 1868.

6 Allbutt, Sir Clifford. Remarks on a Case of Locomotor Ataxia with Hydrarthrosis. *St. George's Hosp. Rep.* **4** 259, 1869.

7 Buzzard, T. Progressive Locomotor Ataxia with Anomalous Joint Affection, *Lancet* **2** 261, 1874.

8 Thompson. Case of Asynergia with Arthropathy, *N. Times & Gaz.* **2** 151, 1877.

9 Schultze, F., and Kahler, O. quoted from Leede, C. S. Arthropathien bei Syringomyelie. Munich, 1908.

10 Schlesinger, H. Die Syringomyelie, ed. 2. Leipzig, 1902, pp. 93-140.

11 Packard, quoted by Mitchell, S. W. *Tr. Path. Soc. Phila.*, October, 1863.

12 Mitchell, S. Weir. Injuries of Nerves and Their Consequences, Philadelphia, F. B. Lippincott Company, 1872.

13 Mitchell, S. Weir. The Influence of Rest on Locomotor Ataxia, *Am. J. M. Sc.* **66** 113, 1873.

14 Chipault, A. Arthropathies nerveuses, arthrites sèches, corps étrangers articulaires traités de chirurgie clinique et opératoire. Paris: Le Dentu et Delbet, 1866, vol. 3, p. 435.



arthritis of the elbow in a patient whose brachial plexus was compressed by callus formed in connection with a broken clavicle

Bowlby<sup>15</sup> cited cases of Blum, Ogle and Arnozan, in which there were changes in the bone following nerve injuries. The chief alteration, however, seemed to be a simple atrophy of the osseous tissue such as might result from disuse. Bowlby stated that he had seen no cases and concluded that they are of rare occurrence. Hirsch<sup>16</sup> described a case of atrophy of the bone following an injury to the median nerve of the arm. Goldscheider<sup>17</sup> reported a case of atrophy of the bones of the hand following disease of the ulna nerve. Fleishhauer<sup>18</sup> cited a case of atrophy of the bones of the foot which developed three months after a traumatic neuritis of the peroneal nerve. Maliwa<sup>19</sup> reported several cases of atrophy of the bones of the hands, especially the phalanges, following nerve injuries. Lehmann<sup>20</sup> described six cases of atrophy of the bones of the hands following nerve injuries, and two cases of atrophy in the os calcis following injury to the sciatic nerve. Campbell<sup>21</sup> observed a case of atrophy of the bones of the foot, following an injury to the posterior tibial nerve. Nonne<sup>22</sup> has observed atrophy of bones within four weeks after a nerve lesion, while Kohler<sup>23</sup> has described it as often occurring within eight weeks after injury to the nerve.

McArdle<sup>24</sup> stated that he has seen arthritic changes when a nerve trunk has been pierced, rubbed or lacerated. These changes have never been seen when a peripheral nerve has been severed unless the nerve ends became bulbous or were caught in healing tissue.

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15 Bowlby, A. A. Some Trophic Lesions Following Injuries of Nerves, *Illus Med News* 4 25, 1889

16 Hirsch, Karl. Ueber einem Fall von Medianusverletzung mit seltenen trophischen Storungen, *Deutsche med Wchnschr* 32 799 and 837, 1906

17 Goldscheider. Ueber neurotische Knochenatrophie und die frageder trophischen Funktionen des Nervensystems, *Ztschr f klin Med* 60 1, 1906

18 Fleishhauer, Kurt. Ueber Nervenverletzungen, *Berl klin Wchnschr* 52 213 (March) 1915

19 Maliwa, Edmund. Trophische Storungen nach Verletzung peripherer Nerven mit besonderer Berücksichtigung der Knochenatrophie, *Med Klin* 26 and 27 704 and 733, 1917

20 Lehmann, Walter. Beitrage zur Kenntnis der sekretorischen und vasomotorisch-trophischen Storungen nach Nervenschüssen, *Med Klin* 23 629 (June) 1917

21 Campbell, Harry. The Trophic Lesions, *Oxford Medicine*, New York, Oxford University Press, 1921, vol 6, p 821

22 Nonne, M. discussion of Sudeck. *Neurol Centralbl* 21 376, 1902

23 Kohler. *Fortschr a d Geb d Rontgenstrhle* 12 41 1905

24 McArdle, J. B. Joint Troubles Arising from Nerve Diseases, *Practitioner* 45 174, 1915

Duncan<sup>25</sup> reported a case of neuropathic arthropathy of the wrist following a peripheral nerve injury. Four years prior to examination a log had fallen on the right shoulder of the patient. In the interim there had been persistent pain in the right arm which the patient had thought to be rheumatism. Duncan believed that the original injury to the shoulder had torn some of the lower cervical and upper thoracic nerve roots. The motor roots apparently were unaffected, for the patient had no impairment in the use of the arm.

Philips and Rosenheck<sup>26</sup> reported two cases of neuropathic arthropathy of the shoulder due to peripheral nerve lesions. The first patient carried heavy blocks of ice on his shoulder, this prolonged muscular strain was thought to be the causative factor. The second patient, who carried timbers in his laboring work, was injured by one of these falling on his shoulder, and he was unable to return to work for ten months. The roentgenograms in both of these cases showed the changes typical of Charcot joints.

Henderson<sup>27</sup> stated that arthropathies of this character are not found in peripheral neuritis, except in those forms closely related to tabes. Campbell<sup>21</sup> has written that the neuropathic joints are rare in peripheral neuritis. Teissier<sup>28</sup> described a case of neuropathic arthropathy which he believed was undoubtedly of the same nature as a Charcot joint occurring in lead poisoning. A sclerosis of the cord was present but peripheral neuritis, which doubtless existed, was not mentioned.

Potter<sup>29</sup> wrote that changes in the bones are frequent with leprosy and referred to a case of Harbitz, in which the phalanges were largely destroyed. Campbell<sup>21</sup> said that changes in the bone may occur in leprosy. Henderson<sup>27</sup> stated that these conditions are not found in leprosy when there is a degeneration of the peripheral nerves. Turney<sup>1</sup> said that the weight of evidence is in favor of Charcot's arthropathies occurring in leprosy, and that this is the only disease of the peripheral nerves in which it is found. He further added that the explanation of this lies in the extreme chronicity of the disease associated with analgesia.

25 Duncan, J. H. Neuropathic Arthritis, *J. A. M. A.* **79** 1987 (Dec. 9) 1922.

26 Philips, H. B. and Rosenheck, C. Neuro-Arthropathies. A Consideration of the Etiology and General Characteristics with Especial Reference to that Form Caused by Peripheral Nerve Disease or Injury. *J. A. M. A.* **82** 27 (Jan. 5) 1924. Neuro-Arthropathies of Peripheral Nerve Injury. Origin. Two Cases. *ibid.* **86** 169 (Jan. 16) 1926.

27 Henderson, V. E. Joint Affections in Tabes Dorsalis. *J. Path. & Bact.* **10** 211 1904-1905.

28 Teissier, M. I. *Lyons med.* **54** 193 1887.

29 Potter, H. E. X-Ray Findings in Neuropathic Joints. *J. Nerv. & Ment. Dis.* **45** 449 1917.

of the deep tissues, which is combined with unimpaired muscular power, precisely as in tabes or syringomyelia

J K Mitchell, Jr,<sup>30</sup> at the close of the Civil War, called attention to the influence of the nervous system on joint lesions, and reported several cases in which neuropathic arthropathies developed after injuries to the spinal cord as a result of gunshot wounds of the spine. Riedel's<sup>31</sup> case is the one most frequently cited to exemplify these joint lesions after injury to the spinal cord. The patient suffered a stab wound between the first and second lumbar vertebrae. This was followed by a paralysis and loss of sensation in one of the legs. Soon after the return of power to some degree, the patient tried to go about and developed an arthropathy of the knee joint. He was able to walk on the leg eight days after the injury. Charcot<sup>32</sup> mentioned the development of these lesions in injuries of the spine, as did Chipault.<sup>14</sup> Albee<sup>4</sup> described these joint lesions occurring after crushing injuries to the cord. Steindler<sup>33</sup> said that in rare instances these joints follow injuries of the spinal cord.

Hildebrand<sup>34</sup> reported the case of a patient with a congenital malformation of the spine, namely, a spina bifida occulta, who developed arthropathic changes. Steindler<sup>33</sup> stated that in rare instances these arthropathies may be associated with malformations of the spine, but failed to state whether or not these are congenital.

Chipault<sup>2</sup> mentioned tumors of the cord and meninges as a possible cause of neuropathic arthropathies. Albee<sup>4</sup> included tumors of the cord in his classification of these conditions.

J K Mitchell<sup>35</sup> was the first to describe the development of these joint lesions following tuberculosis of the spine. He reported four cases in which arthropathies developed below the point at which the spine was affected. This was the first conception of trophic centers controlling the nutrition of bones and joints and antedates by thirty-

30 Mitchell, J K, Jr. Remote Consequences of Injuries of Nerves, and Their Treatment. An Examination of the Present Condition of Wounds Received 1863-1865, with Additional Illustrative Cases, Philadelphia, Lea Brothers & Company, 1895.

31 Riedel, B. Nervenverletzung der linken unteren Extremität, rapide destruction des linken Kniegelenkes durch Gehversuche, Berl klin Wchnschr 20 252, 1883.

32 Charcot, J M. Leçons sur les maladies des systèmes nerveux, 1883, p 111.

33 Steindler, A. Charcot Joints, Journal-Lancet 47 493 (Nov) 1927.

34 Hildebrand, O. Ueber neuropathische Gelenkerkrankungen, Arch f klin Chir 115 443 (March) 1921.

35 Mitchell, J K. On a New Practice in Acute and Chronic Rheumatism, Am J M Sc 8 55, 1831.

seven years Charcot's description of these joints in tabes Gull<sup>36</sup> (1858) reported a case of an arthropathy of the right knee following tuberculosis of the cervical spine This has been mentioned as one of the causes of these joints by Charcot<sup>32</sup> Turney<sup>1</sup> Goodhart,<sup>3</sup> Chipault<sup>2</sup> and Albee<sup>4</sup>

Magnier<sup>37</sup> described these joints in acute myelitis This cause has also been mentioned by Goodhart<sup>3</sup> and Albee<sup>4</sup>

Turney<sup>1</sup> said that these joints are found comparatively rarely in anterior poliomyelitis He further added that the atypical cases of anterior poliomyelitis which present all gradations up to transverse myelitis, are the ones most likely to show these bony changes Nonne recorded a case of marked atrophy of the bones of the foot and tibia four weeks after the onset of the disease, in a boy aged 10 The anterior tibial and peroneal nerves were the ones most affected Goodhart and Albee have given this condition as one of the causes of neuro-pathic lesions of the joints and bones

Turney<sup>1</sup> and Goodhart<sup>3</sup> described these joints in progressive muscular atrophy and amyotrophic lateral sclerosis Osler<sup>38</sup> considered the latter disease to be the spastic type of progressive (central) muscular atrophy Nonne<sup>22</sup> recorded two cases of osseous atrophy in chronic poliomyelitis, which condition is generally accepted to be the Aran-Duchenne type of progressive (central) muscular atrophy

Dementia paralytica has been mentioned by Barker<sup>39</sup> as a causative factor in these bone and joint lesions

Hemiplegia following cerebral hemorrhage was first mentioned as a cause for arthritis by Scott Alison<sup>40</sup> Dejerine and Theohari<sup>41</sup> described a hemiplegic patient who developed a neuropathy of the bones Campbell<sup>21</sup> said that the shoulder joint is the most often affected in these hemiplegic patients who show changes in the bones and joints Albee<sup>4</sup> included this in his classification

Turney<sup>1</sup> and Albee<sup>4</sup> grouped the neurotrophic lesions of bones and joints into (1) osteopathies, (2) arthropathies and (3) osteo-arthropathies

The osteopathies include the spontaneous, painless fractures The changes are increase in the size of the medullary canal decrease in the

36 Gull, Sir W. *Guy's Hosp. Rep.* 4 206 1858

37 Magnier quoted from Turney 1859

38 Osler Sir William *The Principles and Practice of Medicine* ed 8 New York D Appleton and Company 1919

39 Barker L F *Joint Affections in Nervous Diseases*, J. A. M. A 48 384 (Feb 2) 1907

40 Alison, Scott quoted from Turney *Lancet* 1847

41 Dejerine and Theohari *Sur l'atrophie des os du cote paralysé dans l'hémiplégie de l'adulte* *Compt. rend. Soc. de biol.* 5 203 1898

thickness of the compact bone and diminution of the lime salts. Occasionally union of the fracture takes place under the shelter of an enormous amount of callus, and then gives way without apparent cause, except the absorption of the new material.

The arthropathies appear most often in the joints which have been previously damaged, in which a slight injury will precipitate an attack. The changes may be atrophic or hypertrophic. In the ball and socket joints, such as the hip and the shoulder, the atrophic factor predominates, whereas in the hinge joints such as the knee and the elbow, the hypertrophic factor predominates. In tabes, joint symptoms occur in from 3 to 4 per cent of the patients, while in syringomyelia they are present in from 10 to 40 per cent of the cases. Of the tabetic arthropathies, the lower extremities are affected in 75 per cent of the patients, while in those due to syringomyelia, the upper extremities are affected in 80 per cent of the cases. Albee<sup>4</sup> has stated that in the hypertrophic type the articular cartilage disappears leaving bare the porous, cancellous bone with a few peripheral bony outgrowths in some cases. The ligaments and capsule are relaxed and distended with clear fluid. The synovial membrane is either thickened or partially destroyed together with the internal lateral ligaments.

The osteo-arthropathies most often involve the spine and the feet. In the spine the most usual lesions are kyphosis, scoliosis and spontaneous fractures. In tabes the lumbar spine is most often affected, while in syringomyelia it is the cervicodorsal spine, the feet may be flat, deviated outward or inward, or the arches may be raised.

Potter<sup>20</sup> has given an excellent description of the changes shown in the roentgenograms of these joints. The bone margin is irregular, spongy and fringed. Irregular islands of detached bone are found in the interspaces. The osteophytes lie as irregular plaques of bone in the tissues. These are partly formed from pieces of fragmented bone and partly from the cortex of the contiguous joint structures. There is an increase in the lime content of the bone near the joint.

Turney<sup>1</sup> stated that the disease of the ankle joint tends to assume the hypertrophic rather than the atrophic form. The tibia and fibula including the malleoli become quickly overlaid with periosteal deposits. This is the osteoplastic periostitis described by Targett,<sup>42</sup> and the parosteal bone mentioned by Potts.<sup>13</sup> Targett<sup>42</sup> stated that the cavity of the normal articulation of the ankle joint commonly extends at the expense of its smaller neighbors until most of the tarsal joints may be

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42 Targett, J. H. On the Tabetic or Trophic Foot, *Tr. Path. Soc. London* 48: 288, 1897.

43 Potts, W. J. Pathology of Charcot Joints, *Ann. Surg.* 86: 596 (Oct) 1927.

included within it. Chipault<sup>14</sup> described a cavity in the middle of the ankle joint resulting from a disintegration of the astragalus and the os calcis. Barker<sup>39</sup> said that the hypertrophic changes are more common in the ankle and that there is usually an enlargement of the tibia and fibula. Henderson<sup>27</sup> also mentioned the fact that the changes in the ankle are almost always associated with general enlargement of the lower ends of the tibia and fibula. He added that a fracture of the os calcis or astragalus often occurred associated with a high degree of disorganization of the joint. A marked osteophytic production, however, was not common. Rotter<sup>44</sup> reported a case in which within three weeks of the onset of the swelling in the ankle, the joint was so disorganized from persistent use that the external malleolus touched the ground. Turney<sup>1</sup> believed that the hyperplastic element in these nervous arthropathies may be regarded of primarily local origin and that it is a reaction to chronic trauma. It finds its analogue in the various forms of chronic arthritis, expressing a reaction to the irritative processes initiated within the joint.

Turney<sup>1</sup> thought that the seat of the disease in trophic conditions of joints was in the bone, and that any change in the cartilage was subsidiary. The mere presence of the atrophy of the bone is not characteristic, for roentgenograms have proved that it occurs in every case of prolonged or severe articular inflammation. The early appearance and the degree of this atrophy are the important factors in the neuropathic joints. The true explanation of this initial trophic change in the bone is not sensory paralysis but sensory irritation. There is ample reason clinically in regarding the osseous change underlying the group of nervous arthropathies as connected with the irritation of nerves or nervous centers. The nature of this atrophy was shown by Raymond and Onanoff<sup>45</sup> to be a reaction in the nature of a reflex. They set up suppurative inflammation in two corresponding joints of a rabbit having previously divided the posterior roots on one side only. Muscular atrophy appeared as usual on the intact side but remained absent on the side on which the posterior roots had been divided. The experiment was repeated by Hoffa<sup>46</sup> with the same result. Roentgenograms have shown that a reflex atrophy of bone in these circumstances is induced at the same time and in the same way as the reflex atrophy of muscle. It consists of a rarefaction of both the cancellous and the compact bony tissues, and extends far beyond the actual vicinity of the joint. There is special significance in the fact that this change in the bones is also found apart from any joint lesion in cases of injury to peripheral

<sup>44</sup> Rotter, Josef. Die Arthropathien bei Tabes. Arch. f. Klin. Chir. **36** 1 1887.

<sup>45</sup> Raymond and Onanoff quoted from Turney.

<sup>46</sup> Hoffa quoted from Turney.

nerves, which are of partial nature and associated with persistent irritation. It is fairly certain that a division of the nerve per se does not produce changes in bone, except so far as it causes paralysis. The effective cause is the partial division of the nerve, resulting in prolonged irritation.

Tinel<sup>47</sup> and Tuiney<sup>1</sup> agreed that all trophic and vasomotor disturbances are more frequent and severe in neuritic irritations than in simple division of nerves. Goodhart<sup>2</sup> believed that the vascular changes produced by an irritative nerve lesion are the real cause of the so-called "trophic disturbances," and that prompt relief from the irritation becomes an imperative measure to prevent complications. Campbell<sup>21</sup> stated that an incomplete nerve section is most likely to produce these changes in the bone, and that experiments have shown a rarefaction of bone after section of the nerves. He considered that the rarefaction occurring secondarily to nerve injuries is partly trophic in origin, the result of the disturbed vasomotor activity.

Henderson<sup>27</sup> said that observations on the nerves point to lesions of the terminal sensory nerves only. Pitres<sup>48</sup> and others, who worked particularly with the nerves to the joints, have shown a degeneration of the nerve fibers, however, there also have been demonstrated some regeneration and an increase in the nuclei in the bundles.

Eloesser's<sup>49</sup> experiments on cats showed that an arthropathy of this type could be produced in a traumatized joint which had been desensitized. He severed the posterior sensory roots of the cord which supplied the extremities. Tabetic fractures and arthropathies were produced in healthy animals. In the joints of three animals, whose limbs had previously been rendered anesthetic by a section of the posterior roots, following operative trauma there rapidly developed Charcot lesions. These observations are in accord with the statement of Philips and Rosenheck<sup>50</sup> that any joint deprived of its sensory mechanism and subject to trauma may become a typical Charcot joint.

Turney<sup>1</sup> found that experimental sections of nerves in animals have given the most contradictory results. Even when changes in the bones have been found, the conditions have been complicated so much by open sores or by paralysis, or by both, that no conclusions can safely be drawn. Eloesser<sup>49</sup> noted in his animals that many of the joints were infected, especially the ankle, he considered that these resulted from tabetic ulcers developing on the feet.

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47 Tinel, quoted from Goodhart (footnote 3)

48 Pitres, A., and Carrierre, G. *Arch. klin. de Bordeaux* 5 483, 1896, *Rev. neurol.* 4 748, 1896

49 Eloesser, L. On the Nature of Neuropathic Affections of Joints, *Ann. Surg.* 66 201 (Aug.) 1917

50 Philips and Rosenheck (footnote 26, first reference)

The following case report of a neuropathic arthropathy of the ankle joint is presented because of the unusual opportunity to correlate the clinical, roentgenologic and pathologic observations and because the evidence appears to be conclusive that the condition is due to a lesion of a peripheral nerve trunk.

#### REPORT OF CASE

*History*—J R H, a white man, married, aged 29, was first seen on March 24, 1928 complaining of weakness and deformity of the left foot and ankle. He stated that on April 2, 1926, two years prior to this time, while working as a brakeman between two freight cars, his left foot became caught between the guard rail and the railroad track. Before he could free his foot, the train moved about 2 feet. The flange of one car wheel crushed the lower part of the left leg, causing three long, gaping lacerations, from the ankle to the knee. No bones were broken. Following the accident there was a severe infection of the soft tissues of the leg which required drainage tubes for four weeks. It took seven months for the wounds to heal completely. At this time, the patient first bore weight on the foot with the aid of crutches. Shortly afterward he returned to his work as a brakeman, with the foot tightly bandaged. He was able to work intermittently for only a month. The foot and leg were markedly swollen. Walking was accompanied with a great deal of pain and an increase in the swelling. The pain, which was most severe on sitting down after walking, was throbbing and would occasionally radiate from the ankle to the knee. The ankle seemed unusually weak. Nine months after the injury, he began to notice a grating in the ankle with a tendency for the foot to turn outward. This had steadily become worse. One year after the accident, he had the feeling on walking that the foot had come out of the socket. Occasionally there was the sensation of the extremity going to sleep. There was slight pain in the hip and knee at times. The pain, touch and temperature sensations were normal except for a slight inability at times to feel cold as well as in the right foot.

The general health of the patient was excellent. He had typhoid fever at the age of 12 and influenza at 18. There had been no operations or previous accidents. There had been occasional attacks of tonsillitis but no attacks had occurred during the last two years. One tooth was extracted because of an abscess five years previous to examination. There had been infrequent colds with no cough or hemoptysis. The appetite had been good, and the bowels moved regularly. There had been occasional bilious spells. He said that he had not had venereal disease or any symptoms of it. He had been generally nervous since the accident. He had always done active work. His wife was living and well and had had no miscarriages. Two daughters and one son were living and well. His mother died of pneumonia. His father was living and well, as were three brothers and two sisters. There was no history of tuberculosis, cancer, insanity, heart or kidney disease in the family.

*Examination*—Physical examination showed an extremely well nourished and developed man who was suffering no pain at this time. He weighed 165 pounds (74.8 Kg), and was 5 feet 9 inches in height. He was intelligent and cooperative. The skin and mucous membranes were normal. There was no general glandular enlargement. The shape of the head and the hair and scalp were normal. The hearing was excellent and the ears presented no teph or discharge. The pupils were equal and regular and reacted to light and in accommodation. The sclerae



and conjunctivae were normal. The ophthalmoscopic examination gave negative results. The nose showed a normal septum with no discharge. There was no tenderness over the sinuses. The teeth were in excellent condition, showing only a few fillings. There was no pyorrhea and the gums were normal. There were small, atrophic tonsils with no injection of the pharynx. The thyroid was not enlarged. The chest was well developed and symmetrical, with normal respiratory excursions. The apex beat of the heart was in the fifth interspace well within the nipple line. The rate and rhythm were normal, and there were no murmurs. The radial pulse was of good quality and synchronous with the heart beat. The blood pressure was 110 systolic and 60 diastolic. The lungs were normal on auscultation and percussion. The abdomen showed no tenderness, muscle spasm or masses. The liver and spleen were not enlarged. The external inguinal rings were normal. There was no evidence of scars on the external genitalia. The testes and epididymes were normal. The knee reflex was slightly exaggerated on the right and normal on the left. The Babinski, Oppenheim and Gordon



Fig 1—Photograph of the lower legs showing the tremendous amount of swelling and edema on the left. Notice the pigmented scar (*A*) marking the site of one of the original draining sinus tracts, and also the prominence of the lower end of the tibia (*B*) with the eversion deformity of the foot.

reflexes were normal, and there was no ankle clonus. The deep reflexes of the upper extremities were normal. The reflex of the jaw was normal. The cremasterics were absent. The abdominal reflexes were weak. There was no curvature of the spine and the motion was entirely normal. The upper extremities and the right lower extremity were entirely normal.

The main point of interest lay in the left lower extremity. There was marked enlargement of the foot, ankle and calf (fig 1). There was an eversion deformity of the foot of about 45 degrees. The soft tissues about the ankle had a distinct doughy feel. The ankle joint showed a marked increase in fluid, however, there was no tenderness, no increase in local heat and no pain on manipulation. Active and passive motion of the ankle brought out a coarse grating. All movements could be actively carried out. Passive eversion from the resting position was about 20 degrees, while passive inversion was markedly increased, being about 60 degrees. Dorsiflexion and plantar flexion were normal. The foot was held in

about 20 degrees equinus. The lower end of the tibia was prominent, while the lower end of the fibula could be palpated only with difficulty. Many small loose fragments of bone could be felt about the malleoli. Sensory examination showed only a slight impairment of light touch with no well defined areas of hypesthesia. The toes and anterior portion of the foot showed no abnormality. There were three irregularly shaped slightly pigmented scars, marking the sites of the old draining sinuses about the anterior lateral and medial aspects of the lower third of the leg. There was one fine scar extending from the anterior part of the lower third upward and laterally around the calf of about 25 cm in



Fig 2—Roentgenogram taken four months after injury, showing a beginning absorption about the anterior portion of the tibia and the os trigonum

length. There were a few dilated veins in the calf. The knee joint was not enlarged and was entirely normal. There was an apparent atrophy of the thigh. There were no enlarged lymph nodes in the groin. The left ankle was 12 cm larger in circumference than the right. The left calf was 9 cm larger than the right in the lower third and 3 cm larger in the middle and upper thirds. The left knee was 1 cm larger than the right while the middle of the left thigh was 4 cm smaller than the right. The patient walked with a marked limp on the left with the eversion deformity of the foot becoming much more marked. The weight which normally should be borne on the os calcis was taken by the end of the tibia.

The laboratory examination of the urine showed a clear amber color, an acid reaction, a specific gravity of 1.030, no albumin or sugar and microscopically an occasional epithelial cell and leukocyte. The examination of the blood showed 79 per cent hemoglobin, 4,270,000 red cells, and 5,900 white cells per cubic millimeter, of which 55 per cent were polymorphonuclears, 38 per cent large lymphocytes, 3 per cent mononuclears, 2 per cent eosinophils and 2 per cent endothelial cells. The Wassermann reaction of the blood and the Kahn tests were negative. The spinal fluid was of a clear color, came out under normal pressure, had 2 cells per cubic millimeter and gave a negative reaction to globulin and Wassermann tests.

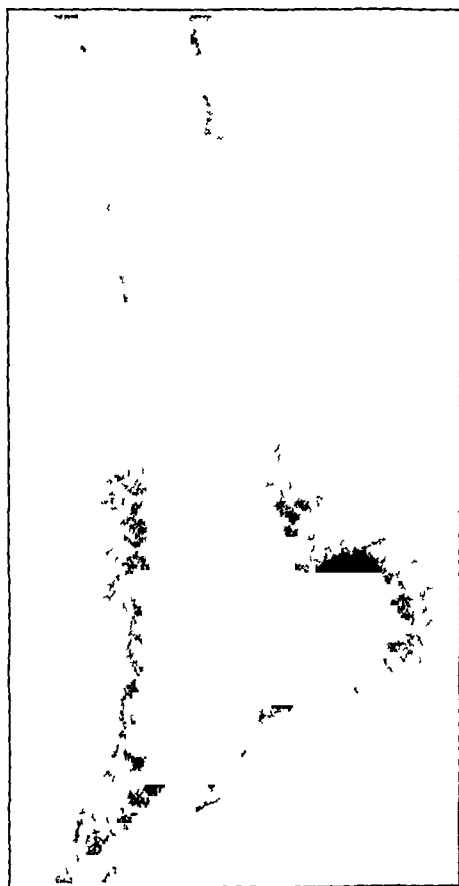


Fig. 3—Roentgenogram taken nineteen months after injury, showing an almost complete absorption of the body and neck of the astragalus, with a disintegration of the upper surface of the os calcis and the lower margins of the tibia and fibula, and numerous loose fragments of bone about the joint.

The joint fluid from the left ankle had a slightly reddish tinged cloudy appearance and contained 32,200 cells per cubic millimeter, of which 51 per cent were polymorphonuclears, 41 per cent lymphocytes, 2 per cent basophils and 6 per cent mesothelial cells. Both the Wassermann and the Kahn tests on this fluid were negative. Two separate cultures of this fluid showed the presence of *Staphylococcus albus*, which took three days to appear on the culture mediums on the first

occasion and four days on the second occasion. In aspirating the joint with a large sized needle there was the complete absence of pain as soon as the skin had been penetrated.

The roentgen examination of the left ankle, taken in August, 1926, four months after the injury (fig 2) showed the calcification through the neck and anterior portion of the astragalus not to be as uniform as normal. There was a definite area of absorption in the os trigonum. There was an irregularity and beginning separation of the lower anterior tibial margin. There was a slight amount of atrophy through all the bones of the lower part of the leg and ankle. The outline

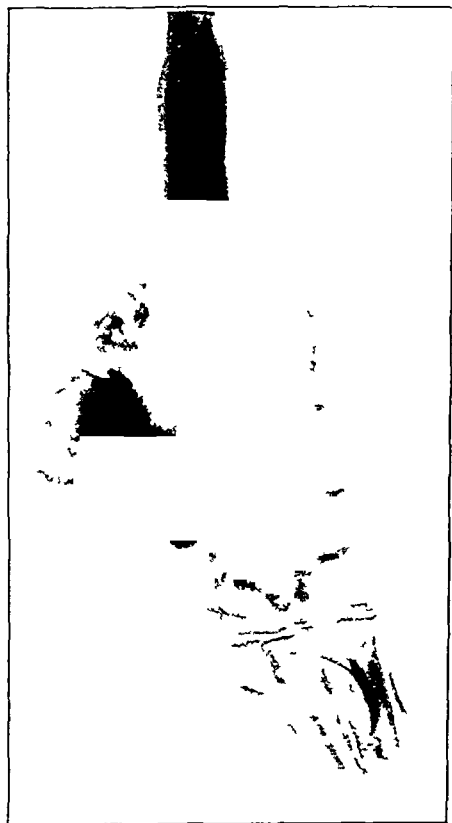


Fig 4—Roentgenogram taken twenty-three months after the injury, showing a more marked absorption and disintegration than in figure 3 with many more loose irregularly shaped bone fragments. There is also a proliferation of bone along the cortex of the fibula and a separation of the astragaloscaphoid joint.

of the soft tissues showed a large amount of swelling. The roentgenogram of the left ankle, taken in November 1927, nineteen months after the injury (fig 3), showed a marked disintegration of the tibio-astragalar and astragalocalcanean joints. There had been a complete absorption of the body and neck of the astragalus. There had also been an absorption of the upper portion of the os calcis and the lower margins of the tibia and fibula. There was an osteosclerosis of the margins of the tibia and fibula and the upper portion of the os calcis.

There were many large and small, irregularly shaped masses of bone in the soft tissues surrounding the disintegrated areas. There was bone proliferation along the cortex of the tibia and fibula, extending for a distance of several inches up the shafts of these bones. There was also an irregularity about the posterior margin of the scaphoid and the anterior margin of the remaining portion of the head of the astragalus. The outline of the soft tissues showed a more pronounced swelling than on the previous examination. The roentgenogram of the left ankle, taken in March, 1928, twenty-three months after injury (figs 4 and 5), showed the disintegration and changes in the joints previously noted to be more advanced

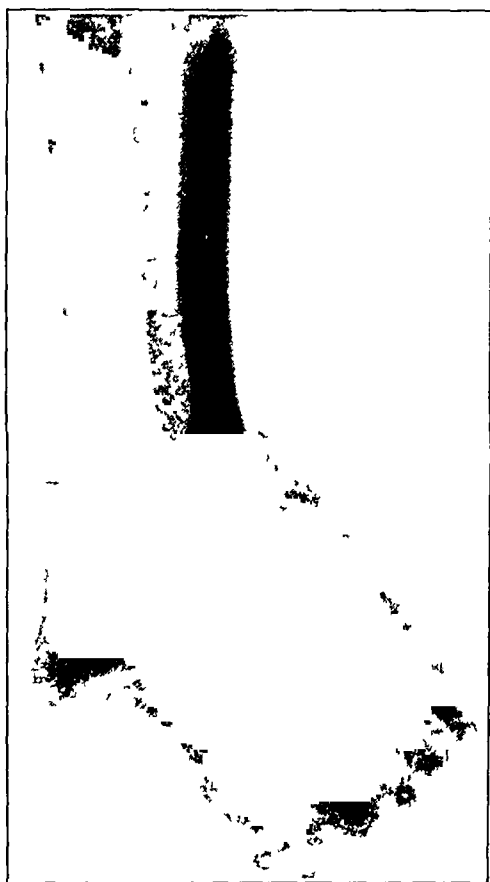


Fig 5—Roentgenogram taken twenty-three months after the injury, showing the marked lateral dislocation of the ankle and foot

There were many more unattached bone fragments about the joint. The disintegration of the astragalus and upper portion of the os calcis was greater. There was a separation of the astragaloscaphoid joint. The bone proliferation along the cortex of the fibula was more noticeable. In the anteroposterior view, there was a marked lateral dislocation of the foot and ankle. Roentgenograms of the lumbar spine, pelvis and hips, taken in March, 1928, showed the bones to be entirely normal. There was no suggestion of a spina bifida or other abnormality.

*Operation*—Operation was performed on March 25, 1928. With the patient under a general anesthetic, the left foot and ankle were amputated in the middle

third of the lower part of the leg. The muscle tissues were found to be extremely boggy and edematous. There were two sinus tracts in the calf muscles: one extended down to a point just above the medial side of the ankle and there terminated in scar tissue, the other extended up into the muscles of the calf to a point about 4 inches below the inner aspect of the knee joint. These sinus tracts did not communicate with each other. They were both filled with the same slightly reddish, cloudy fluid which had previously been aspirated from the ankle. The posterior tibial nerve was demonstrated on the medial aspect of the calf and traced down to a point about 2 inches above the ankle joint, where it terminated in scar tissue. This was adjacent to the termination of the lower sinus tract. A portion of this nerve trunk and a portion of the wall of one of the sinus tracts were removed for pathologic section. The edematous muscle

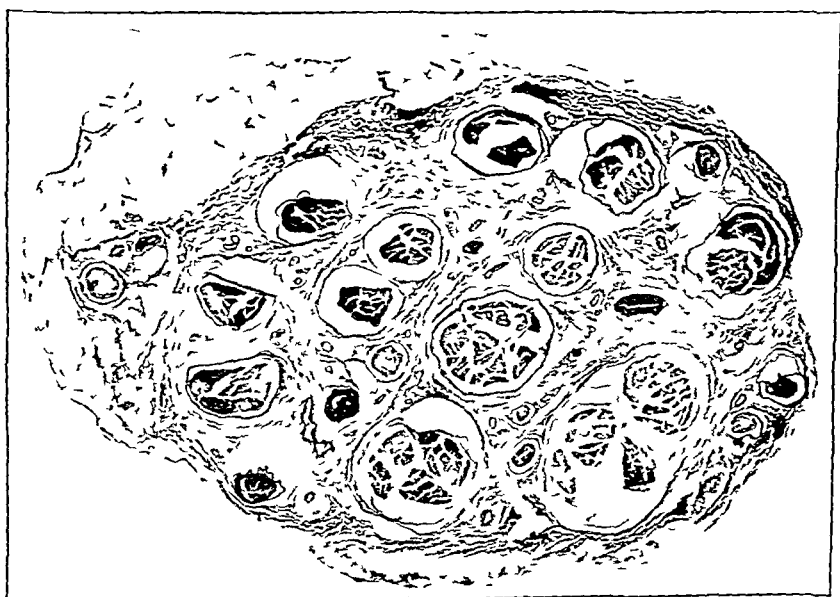


Fig 6—Photomicrograph of the posterior tibial nerve showing an enormous increase in connective tissue between the nerve bundles and a generalized edema

tissue was pulled down over the ends of the bones and sutured. The subcutaneous tissue and skin were closed without tension. One small protective drain was inserted.

After considerable drainage the incision healed in about ten weeks. There was no tendency for the incision to gape. Six months after the amputation the stump had shrunk to about one-half its previous size and the patient was walking with an artificial limb.

*Pathologic Report*—The pathologic report of the tissue removed at the time of operation was as follows: The cross-sections of the nerves showed an enormous increase in the connective tissue between the nerve bundles with a general edema in both the nerve bundles and the connective tissue (fig 6). The cross-sections of the sinus wall showed muscle structure in which there had been a marked replacement fibrosis and myomatous degeneration.

The pathologic report concerning the specimen was as follows (fig 7): When the specimen was opened there was seen a cavity between the lower end of the



Fig 7—Photograph of the specimen, which has been opened *A* indicates the cavity between the lower ends of the tibia and fibula and the bones of the tarsus, *B*, lower end of the tibia, *C*, head of the astragalus, which is the only remaining portion of this bone, *D*, scaphoid, *E*, first cuneiform, and *F*, point at which the posterior tibial nerve was found to terminate in scar tissue

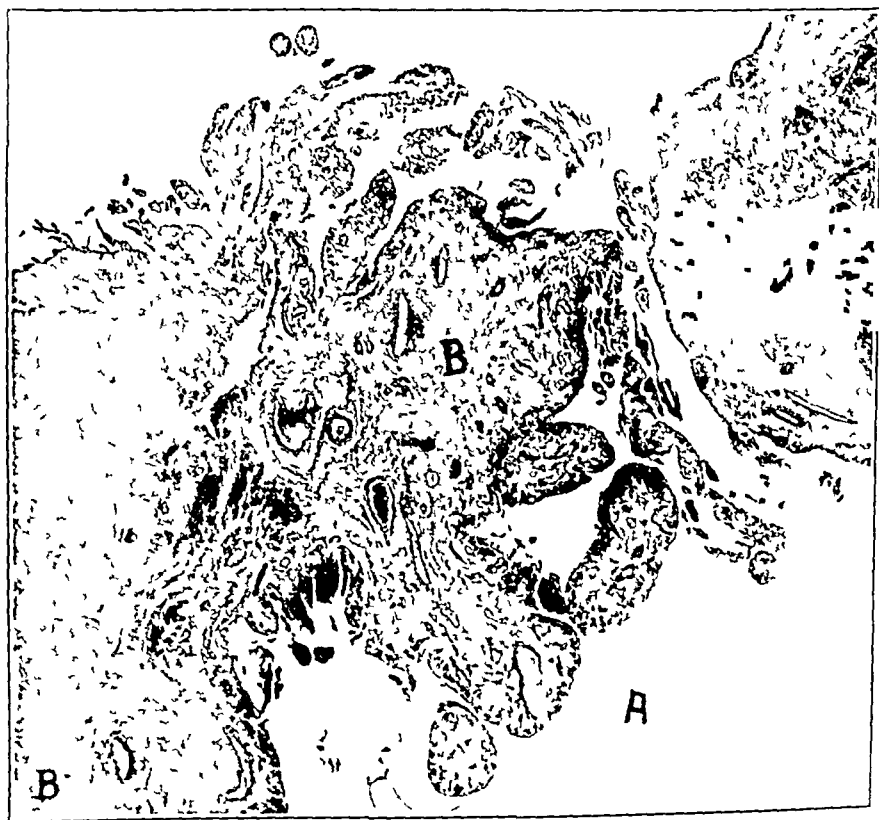


Fig 8—Photomicrograph (low power) showing one of the villus-like projections, which is all granulation tissue (*B*), extending into the cavity (*A*)

tibia and fibula and the bones of the tarsus, irregular in shape, roughly 8 cm in diameter, containing a cloudy, blood-tinged fluid. Extending up the leg apparently originating in or near this cavity, were two sinus tracts, which were rather hemorrhagic on gross examination. There were loose particles of cartilage and bone forming part of the wall of the cavity. The lining membrane was rough with villus-like projections over the various parts of the surface somewhat irregularly placed. The microscopic examination showed these villus projections to be in part cartilage and in part dense fibrous tissue, the nuclei being separated for considerable distances by strands of collagenous fibers (fig 8). The vascular fragmentations were extremely abundant (fig 9), forming granulation-like tissue simulating angioma, while on the actual surface there were masses of fibrin, in which were meshed some hemolyzed blood corpuscles and a few leukocytes, the



Fig 9—Photomicrograph (high power) showing the extremely vascular character (B) of the granulation tissue in the villus projection extending out into the cavity (A)

polymorphonuclear variety predominating. Sections through the bone showed a chronic inflammatory process characterized by replacement of the marrow by fibrinous connective tissue, there being practically no remaining marrow cells in the pieces of bone examined, which included a section from the end of the tibia and smaller masses of bone found about the cavity wall (fig 10). Sections from the sinus in the leg showed dense fibrous tissue replacing muscle surrounding the sinus tract which was lined by hemorrhagic granulation tissue (fig 11). The cells of the capillaries appeared exceedingly active suggesting an angiomatous formation. Grossly nerves had been caught in scar tissue about the sinus and could not be followed through. In the microscopic sections the nerve could not be followed except for a short distance, ending away into fibrous tissue without



the formation of a definite neuroma. Traversing the fibrous tissue were occasional fibers, which presumably represented remnants of nerves (fig 12). The inflammatory reaction was of a relatively low grade, except for the presence of hemorrhage along the sinus and the fibrinous exudate on the lining of the cavity.

#### COMMENT

The majority of the neuropathic arthropathies observed are those joint conditions found in tertiary syphilis spoken of as Charcot joints. This is generally described as a rapid, painless disorganization of the joint structures, due to disease of the sensory nerve tracts supplying this part. Any joint of this type with a suspected etiology of different

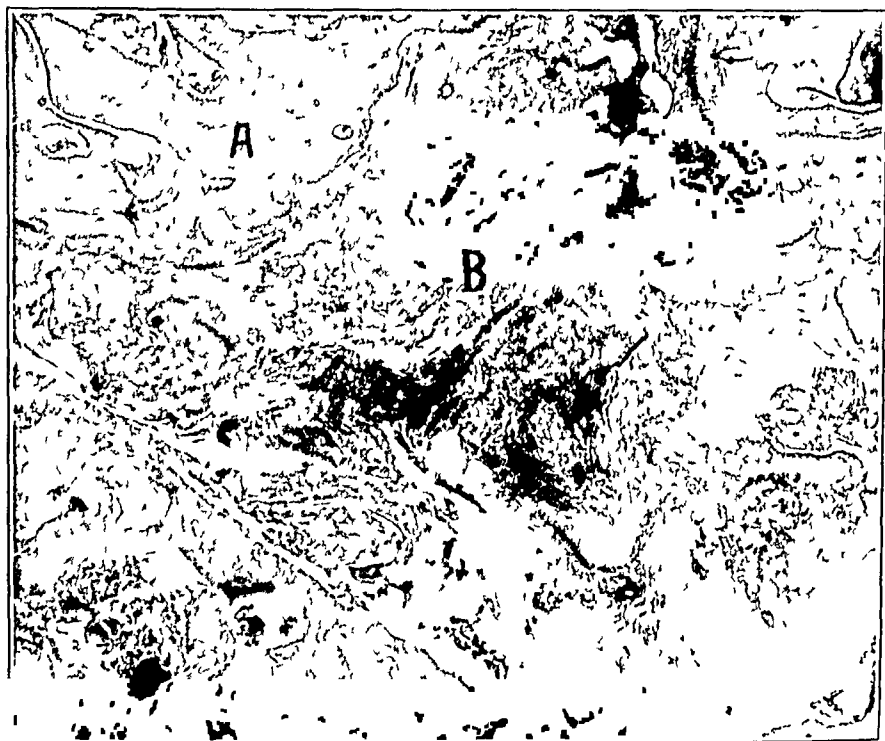


Fig 10—Photomicrograph (low power) showing bone from the end of the tibia. There is noted rather marked bone destruction (*A*) with an invasion of the marrow cavity with inflammatory tissue (*B*).

character should first be proved to have no association with syphilis before this cause can be accepted. In this patient there was no evidence of syphilis, as shown by (1) negative Wassermann and Kahn tests of both the blood and the joint fluids, (2) a negative Wassermann reaction of the spinal fluid, (3) the lack of any history of possible syphilitic infection and (4) the lack of any clinical manifestations of syphilis.

At the time of the amputation of the ankle, the posterior tibial nerve was traced down to a point above the medial aspect of the joint, where it terminated in scar tissue. It was impossible to determine whether

the nerve at this point had been wholly or partially severed at the time of the injury, or whether, following the infection of the soft parts of the leg the nerve trunk also became infected and later was obliterated by scar tissue. In view of the present conception of the development of these neuropathic arthropathies it is most likely that there was either a partial division or an infection of the nerve which resulted in an irritative nerve lesion. The sections of the portion of this posterior

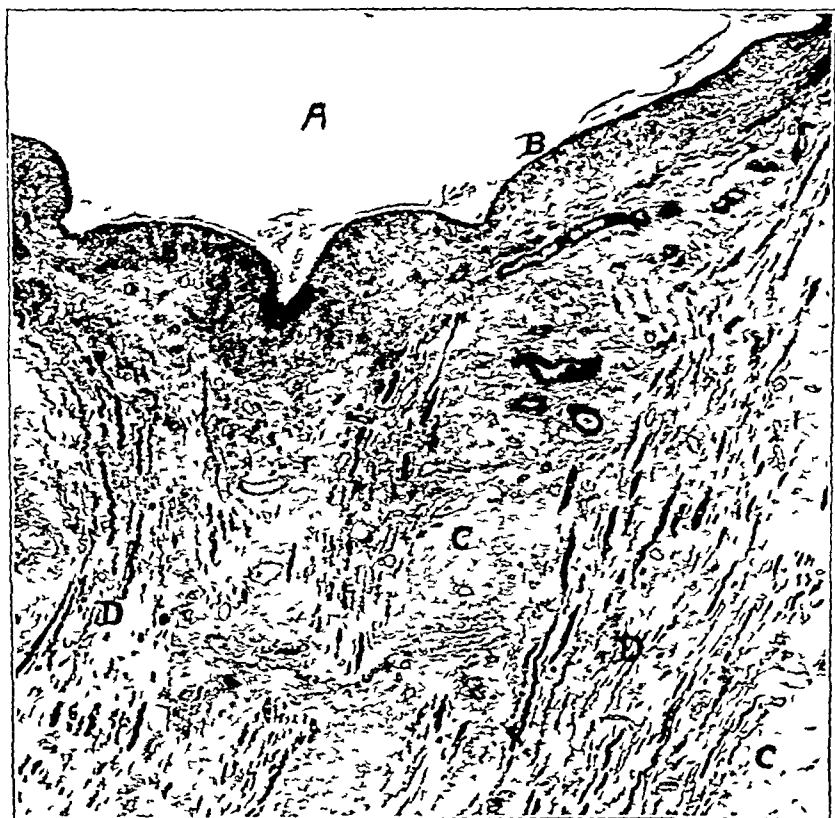


Fig 11—Photomicrograph (high power) showing the wall (B) of a sinus tract (A) with fibrin along margin. A marked fibrosis (C) can be seen surrounding the remaining muscle tissue (D).

tibial nerve removed at the time of the operation show a marked increase in connective tissue between the nerve bundles and a generalized edema (fig 6). The posterior tibial nerve supplies the main articular branches to the ankle as well as to the astragalocalcaneal and the astragaloscapoid joints. With a prolonged irritation of this nerve trunk subsequent changes in the joints supplied would be expected. It is rather interesting to note the circumscribed area adjacent to one of the sinus tracts, distal to the point at which the posterior tibial nerve ended in scar tissue,

shown in figure 12 This resembles a hyalinized nerve bundle, although no definite nerve structure can be made out There were also in the fibrous tissue in this area occasional nerve fibers, which were thought to represent remnants of the original nerves These anatomic evidences of disturbance of innervation of the part point toward a peripheral nerve lesion as being the primary etiologic factor of the arthropathy There

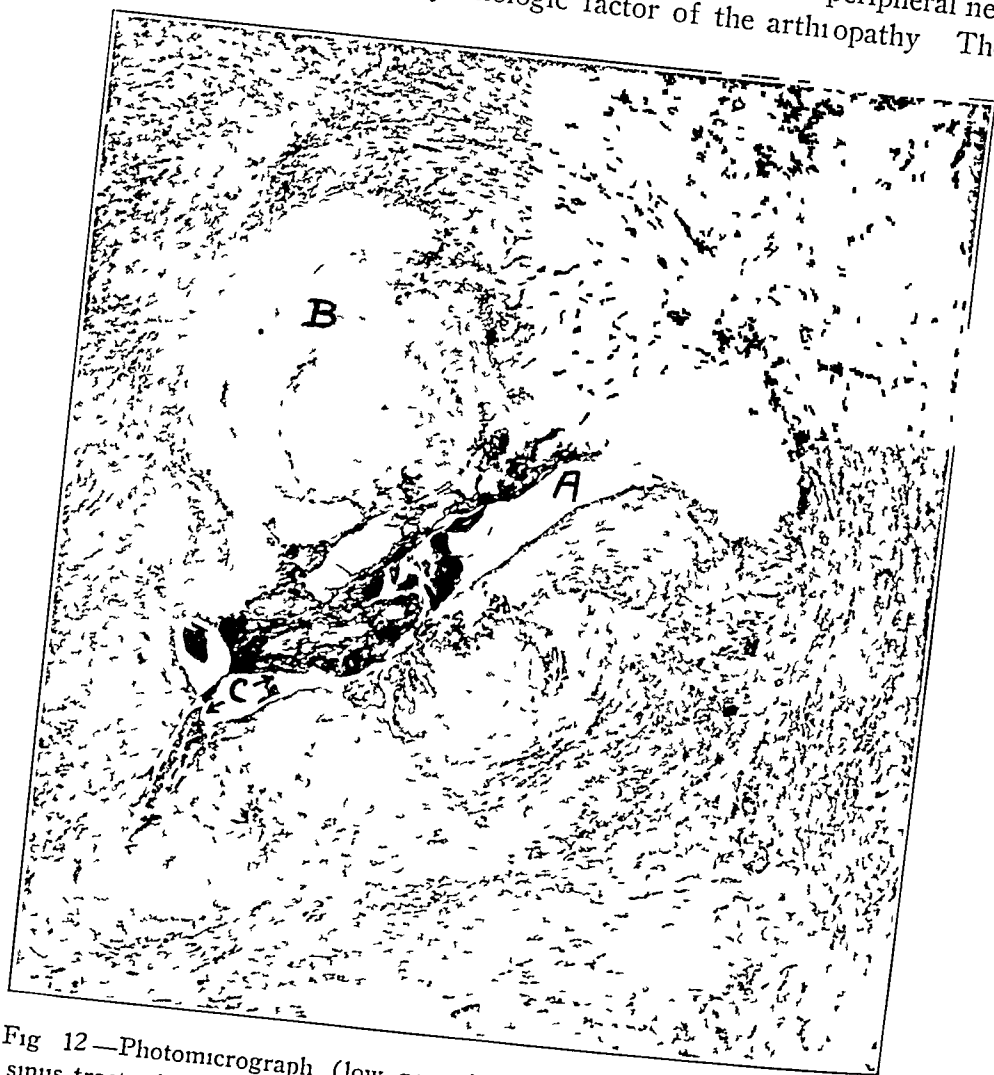


Fig 12—Photomicrograph (low power) showing a cross-section of one of the sinus tracts (A), containing some fibrin (C), adjacent to which is a circumscribed, lighter stained area, which is thought to be a hyalinized nerve bundle (B), although no definite nerve tissue can be demonstrated

were two significant clinical evidences of neurologic character, which showed a disturbance of the sensory mechanism First, the pain in the ankle on weight-bearing and walking was not commensurate with the pain which would be expected to accompany this amount of joint disintegration if the sensory nerves were not involved second, there was

complete absence of pain when the joint structures were pierced with an aspirating needle. The latter is spoken of as Eloesser's<sup>51</sup> sign, but was first described by Oehlecker<sup>52</sup> (1914).

The changes seen in the roentgenograms form an interesting part of the picture. Steindler<sup>33</sup> stated that the x-ray pictures demonstrate small infractions and fissures to be the first changes in these joints. The first roentgenogram of the ankle taken four months after injury shows these early changes (fig 2). At this time, the only trauma the joint had received was that associated with the accident. No weight had been borne on the ankle since injury. Nine months after the accident the patient first started to walk, and it was shortly after this that he noticed a grating as if the ankle were out of place. This weight-bearing on a joint that previously had been almost completely desensitized through an injury to its nervous mechanism was the direct cause of most of the pathologic changes. The experimental work of Eloesser<sup>49</sup> tends to confirm this clinical observation. The second roentgenogram taken nineteen months after the injury shows the changes to be far advanced (fig 3). At this time, the patient had been walking on the ankle for about one year. Four months later, the third roentgenogram presents even more marked changes, with a great many additional plaques of bone about the joint (fig 4). The anteroposterior roentgenogram shows a marked lateral dislocation to be present (fig 5). All of the changes in the bone described by Ridlon and Berkheiser<sup>53</sup> can be seen in these roentgenograms, namely, atrophy of the bone ends, osteoporosis with erosion, osteosclerosis, proliferation of irregularly shaped bone masses and osteophytes. The parosteal bone of Potts<sup>43</sup> or the osteoplastic periostitis of Targett<sup>42</sup> can be observed to extend well up the shaft of the fibula.

The development of the sinus tracts within the calf and the cavity found in the ankle joint are unusual features of the condition. The lower one of these sinus tracts in the calf apparently at one time connected with the cavity in the ankle (fig 7). Targett<sup>42</sup> and Chipault<sup>14</sup> have both described this cavity which forms in the ankle joint with the progressive development of the arthropathy. Rotter<sup>44</sup> reported a case of neuropathic arthropathy in which synovia or serous fluid was removed from the submuscular tissue at some distance from the joint, but did not describe any sinus tract formation. The villus-like projections (fig 8) found in the cavity and sinus tracts apparently were formed by the

51 Eloesser, L. A Sign Occurring in Tabes Complicated by Charcot Joints, *J A M A* **77** 604 (Aug 20) 1921.

52 Oehlecker, F. Ein weiterer Beitrag zur Klinik Unvollbezogachtung und Behandlung tabischer Gelenkerkrankungen. *Beitr z klin Chir* **92** 599 1914.

53 Ridlon, John and Berkheiser, E. J. Neuropathic Arthropathy of Charcot's Spines. *J A M A* **79** 1467 (Oct 28) 1922.

organization of the fibrin. In some of these villi, cartilage cells were found. It is likely that these became enmeshed in the fibrin after sequestration from the joint surfaces as small bits of cartilage. The nutrition in the fluids was sufficient to keep these cartilage cells alive, so that they proliferated to form the small nodules found in the walls of the sinuses and cavity. The lower end of the tibia was found to be covered with cartilage-like tissue, which probably represents an attempted repair of the normal hyaline cartilage. The invasion of the bone-marrow of the lower end of the tibia with fibrous and granulation tissues is what would be expected with these pathologic conditions (fig. 10).

The extensive fibrosis and edema found in the muscle tissue taken from the calf (fig. 11) is in keeping with the gross changes in this part. Through this muscle tissue, as well as through the walls of the sinus tracts, there was a rather extensive vascular proliferation (fig. 9). The two cultures of *Staphylococcus albus* from the joint fluid of the ankle are indicative of an infection. These are not believed to be a contamination because of the slow appearance time on the mediums. The extremely high cell count with a predominance of polymorphonuclears in this fluid also favors the presence of an infection. It is interesting to note the extremely high percentage of mesothelial cells in this fluid, which cells are characteristic in the joint fluid in low grade arthritic infections. This infection is undoubtedly responsible for a great many of the changes through the muscles and tissue in the calf and ankle.

There have been reported instances of neuropathic joints associated with a spina bifida and injuries to the spinal column. This possibility in the patient is ruled out by negative roentgenograms of the lumbar spine and pelvis and a negative history of injury to the lower part of the back.

#### CONCLUSIONS

1. A classification of the neuropathic lesions of the bones and joints is presented.
2. A case of neuropathic arthropathy of the ankle is reported.
3. The etiologic factor in this case appears to be a peripheral nerve lesion, as the posterior tibial nerve was found to terminate in scar tissue above the joint.

# GENITAL PROLAPSE FOLLOWING TOTAL HYSTERECTOMY

A SUCCESSFUL OPERATIVE PROCEDURE \*

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Total removal of the uterus is a definitely indicated surgical procedure for several gynecologic conditions. Vaginal hysterectomy is a development which has followed the necessity of total removal of the uterus. This procedure has become very popular in the average operating room, as the technic is easier than that of the abdominal operation and the mortality rate is much lower. By the abdominal route the problem of supporting the bladder and vault of the vagina is much more readily handled than by the vaginal route.

In the early nineties, Pryor popularized vaginal hysterectomy through the use of his clamps. Since that period a much better operation for the removal of the uterus by the vaginal route was offered by Dr. Charles Mayo and has been adopted more or less universally. In the Pryor operation there was no provision made against the possibility of prolapse of the vagina and bladder other than the perineal supports. In the Mayo operation, the broad ligaments are brought together and the bladder so fixed that vesical and vaginal prolapse is skillfully prevented in the majority of these operations.

However, after any type of vaginal hysterectomy a marked genital prolapse often happens in which the vagina becomes completely everted and the bladder partially or completely protrudes. With the cervix and its attached supports entirely wanting in these cases, the problem of returning the bladder to the abdomen and fixing it there through any type of vaginal operation, is, practically speaking, impossible.

In all the literature and textbooks on this question of genital prolapse after total removal of the uterus the only procedure offered to relieve this trouble is colpocleisis. Simon, in 1885, originally recommended and described colpocleisis for the cure of intractable vesicovaginal fistula, but for the past twenty-five years or more, colpocleisis has been undertaken repeatedly for the cure of genital prolapse after total removal of the uterus. Needless to say, not only is this operation a poor surgical procedure which is rather difficult to accomplish properly and gives a poor result in many instances, but it is definitely disfiguring.

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\* Presented at the Annual Meeting of the Medical Society of Virginia, Charlottesville, Va., Oct. 23, 1929.

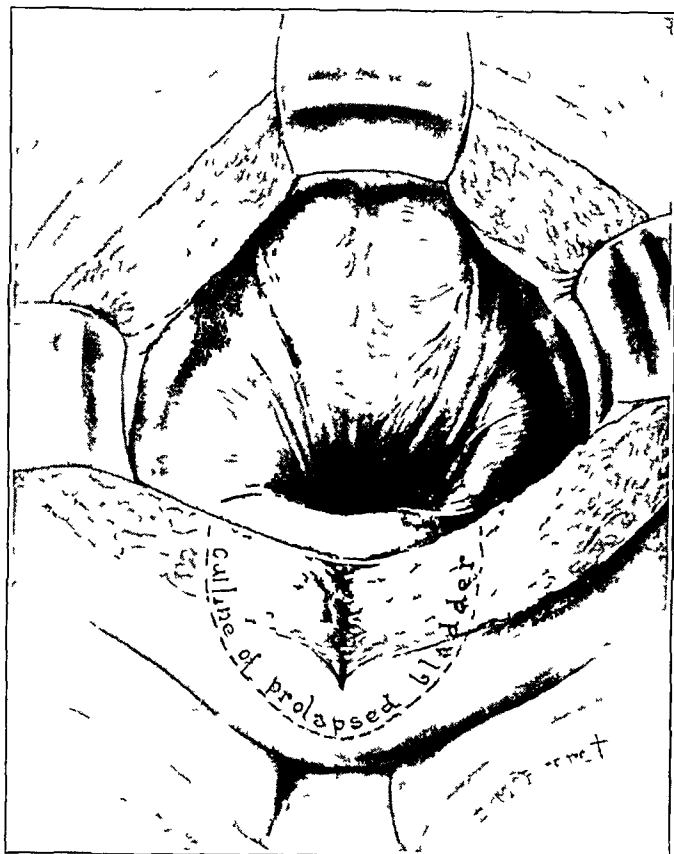


Fig 1—A diagrammatic sketch showing the funnel-shaped appearance of the pelvis when the abdomen is opened and before the bladder and vaginal prolapse have been reduced. It will be noted that the two broad ligaments, consisting of the round and infundibulopelvic ligaments, together with the fibrous structures between, are drawn down and attached to the apex of the funnel the smaller end of which coincides with the upper end of the vagina where the cervix was originally located.

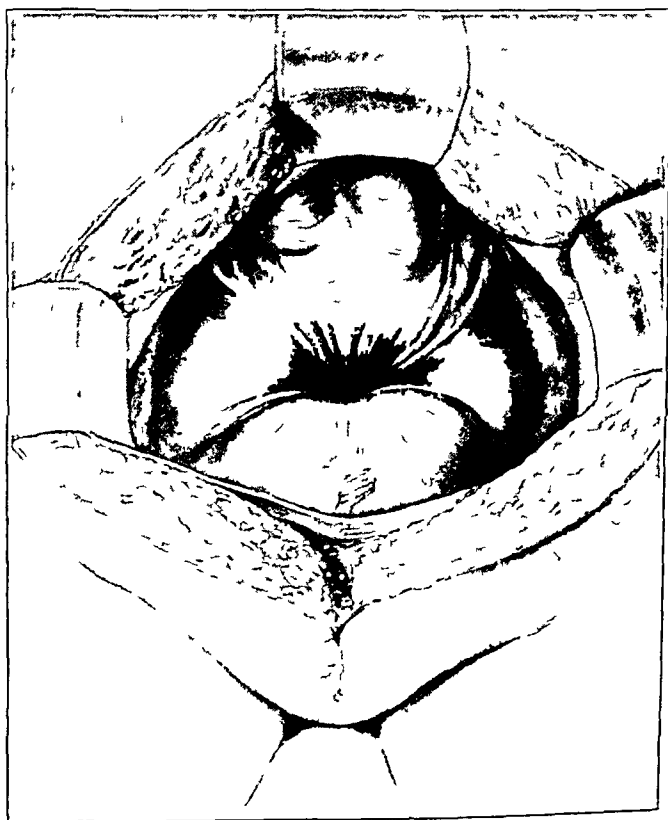


Fig 2—The same relation of the broad ligaments, but the vagina and bladder have been returned to the normal position.

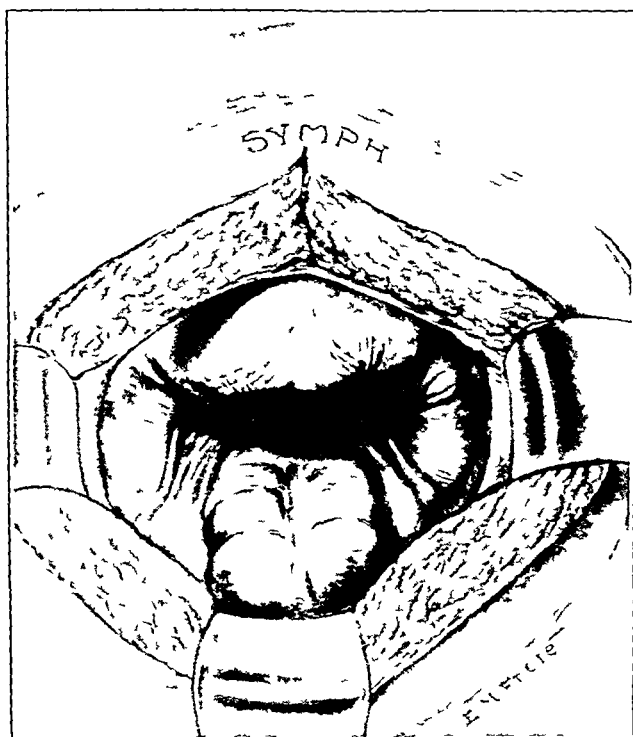


Fig 3—The same relationship of the pelvic structures, with the patient in the Trendelenburg position. It will be noted that the bladder is rolled upward and completely covers the apical attachments of the broad ligaments to the upper end of the vagina.

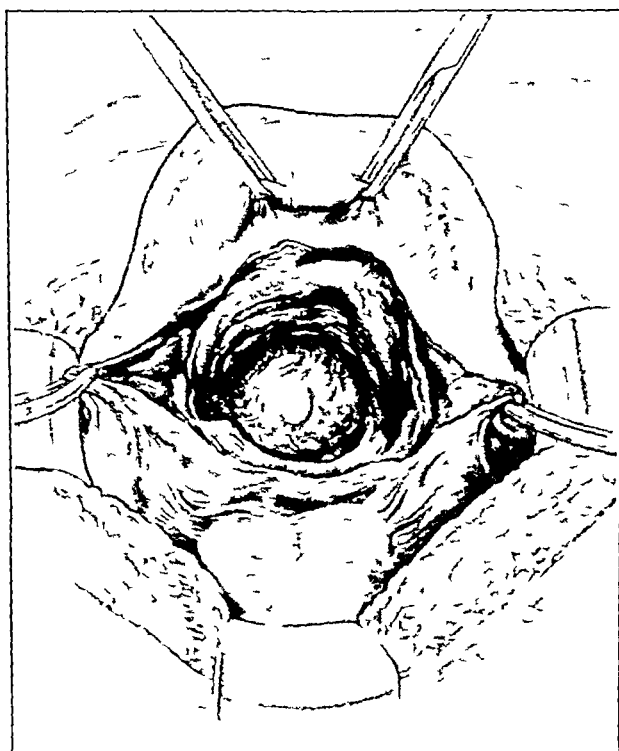


Fig 4—The first step is the introduction of the Cameron light through the vulva to the upper end of the vagina. This acts as a mechanical guide, the glow of the light readily facilitates the identification of structures. The dissection provides for the complete freeing of the bladder anteriorly, the broad ligaments laterally and the rectum posteriorly from the vagina. In the average case the vagina will then represent a raw cone from 1½ to 2½ inches (3.8 to 6.3 cm.) long.



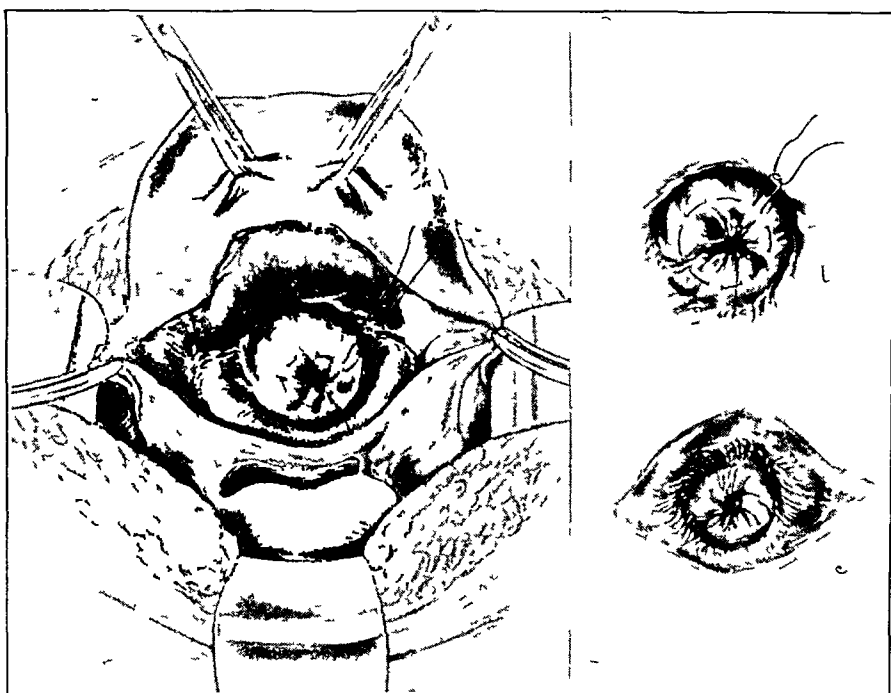


Fig 5—With the pelvic portion of the vagina completely freed on all sides, the next step consists of the introduction of three purse-string sutures of silk, *a*, *b* and *c*. Each purse string is tied before the next one is put in, this results in an infolding mass of the upper end of the vagina which provides a kind of plug for the outlet and at the same time shortens the normal depth of the vagina, depending on its individual length. The average reduction in length is about half



Fig 6—After the infolding of the vagina, the broad ligaments are brought obliquely across the vaginal ball and sutured snugly to fibrous structures on each side of the vaginal stump

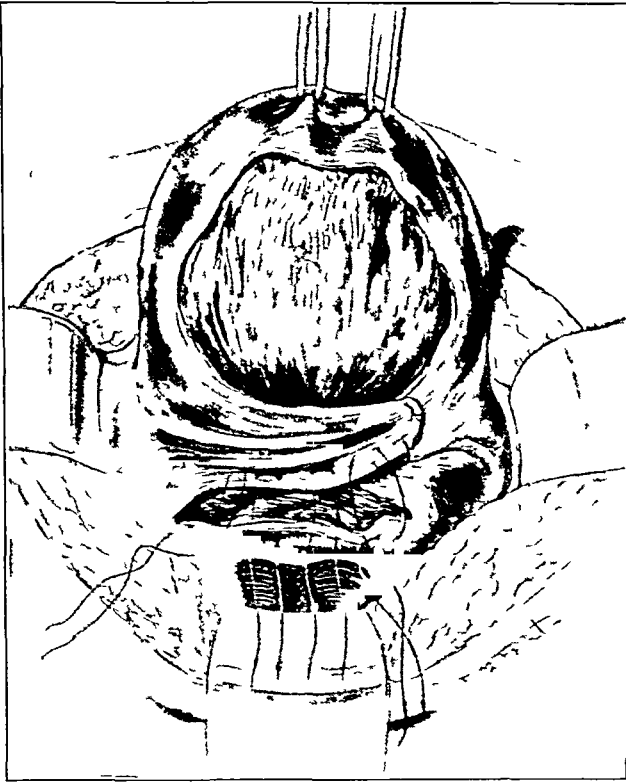


Fig 7—Both broad ligaments are overlapped and snugly sutured behind the bladder and as near to the apex or trigone as is possible, thus providing an additional sling or hammock on which the bladder can be supported

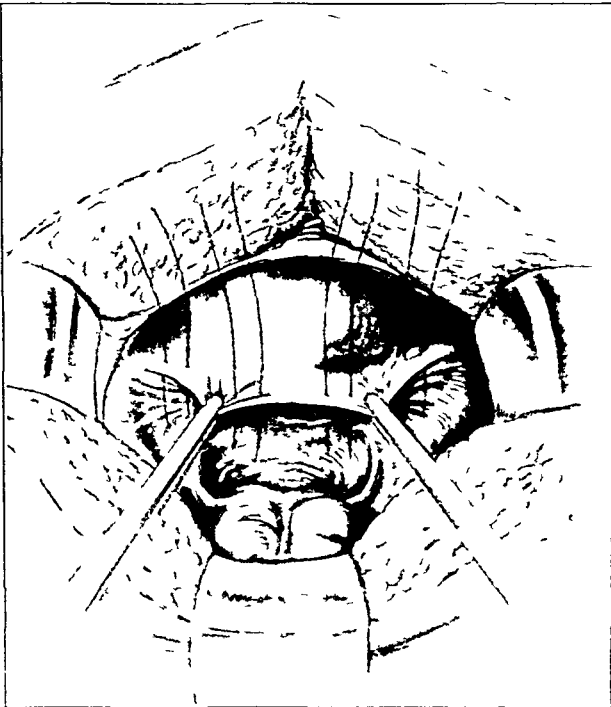


Fig 8—The final step in which the bladder is brought backward over the constructed supports and sutured to the posterior pelvic area in a manner that will cover up all raw surfaces. Following the closure of the abdomen a snug high perineal repair is always done according to the technique previously described (Payne—A Technique for the Repair of Relaxed or Lacerated Perineum. J. A. M. A. 78: 574 [Feb. 25] 1922)

This problem of genital prolapse presented itself to me about fifteen years ago. After obtaining no help from my confrères or from the literature, I finally devised the technic given in the accompanying illustrations and legends. I have done this operation only four times, the last one two years ago and the first one more than ten years ago. In these four cases, the result has been entirely satisfactory. I am describing it here with the hope that it may be of some help to other operators and, through a greater trial of the procedure, thus to determine its value from the standpoint of a temporary or a permanent cure.

This is not claimed to be a new operation, all the steps or principles have been utilized for years in other gynecologic problems. The technic merely covers the application of well known principles which, as far as I can discover, have not been described in the literature or applied to the handling of this particular problem of prolapse after total hysterectomy.

# CHRONIC IDIOPATHIC DUODENAL ILEUS ASSOCIATED WITH HYPERTHYROIDISM

REPORT OF CASES, ONE WITH ANATOMIC OBSERVATIONS \*

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Chronic duodenal ileus or obstruction may be divided into several types. It may be idiopathic, or it may result from some abnormality or pathologic condition, including postoperative complications. Idiopathic ileus may be (1) adynamic or paralytic, (2) dynamic, due to excessive muscle contraction, or (3) mechanical.

Clinically, the course may be persistent, intermittent or remittent.

The location of the obstruction may be in any portion of the duodenum. In this study, however, the nonparalytic type of idiopathic ileus is chiefly considered, with the obstruction at the terminal duodenum.

Numerous theories and predisposing factors have been advanced for this condition, with little supporting evidence. However, no reference has been noted in the literature to the association with hyperthyroidism.

The anatomic postmortem observations in one case add unusual interest.

## REPORT OF CASES

CASE 1—*History*—J. W., a man, aged 39, married, entered the Presbyterian Hospital on March 12, 1926, and was discharged on Sept. 16, 1926. The chief complaints were palpitation of the heart, tachycardia, nervousness and extreme weakness. The patient had two children who were living and well. He was employed in an office and had had considerable business worries during the last few years. He smoked a great deal.

The onset of symptoms began about two weeks previously with tachycardia, which persisted, with attacks of palpitation.

During the first week, he stated that he had an aching and soreness over his body as though he were having grip. During the second week, he was restless at night and had little sleep. He had noticed an enlargement of the neck during the last few days. Weakness had been marked at times and had been accompanied by a feeling that he might collapse. He had lost some weight during the last ten days. His normal weight recently had been about 180 pounds (81.6 Kg.). There had been a tremor of the hands noticeable during the last few days. The appetite had been good.

Many years previous to admission, the patient had two attacks of pneumonia. Rheumatic pains were present for a short time several months before admission.

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\* Submitted for publication Oct. 25, 1929.

to the hospital, after which he had a short vacation, and felt well. He had influenza twice several years prior to the present illness and occasionally had sore throat.

Four years previous to the present admission, he entered this hospital during a subacute attack of appendicitis. In his history, he stated that a few months previously he had experienced two attacks of unusually severe distress following the eating of pork, which nearly always occasioned some distress. This was associated with belching of gas, which lasted one night. There was no other history of stomach or gallbladder trouble. An Ewald test meal was given and showed a free acid of 35 and a total acid of 70. A seven hour motor meal contained about 3 ounces of solids which contained free acid. At that time, I removed a subacutely inflamed appendix and a gallbladder filled with faceted stones. The surface of the liver was gray and thickened. A piece removed at the time showed chronic hepatitis microscopically. There have been no subsequent symptoms of stomach trouble.

*Physical Examination*—The patient was about 6 feet tall and was thin. He was extremely nervous. Exophthalmos was slight, but other eye symptoms of exophthalmic goiter were moderately advanced. The tonsils were hypertrophic and cryptic. Roentgenograms of one tooth showed some evidence of apical infection.

There was a diffuse moderate enlargement of the thyroid gland, including the isthmus. There was a bruit and pulsation over the gland.

The pulse rate was rapid. Auricular fibrillation was present at times.

The abdomen was slightly retracted and tense. The old operative scar was firm.

The extremities were constantly in motion. There was a marked coarse tremor of the fingers. The reflexes were normal.

Results of the examination were otherwise negative.

The course of the hyperthyroidism was unusually severe (fig 1). The heart was dilated, and auricular fibrillation was frequently present. The nervous symptoms were marked. His condition was so serious after four weeks of treatment with a compound solution of iodine that the superior thyroid arteries were ligated at an interval of one week. Almost immediately he became delirious, and the administration of the solution had to be stopped because it aggravated his symptoms. The delirium, which was maniacal at times, continued for about two months. Emaciation became marked, and at times the patient was in a dying condition. He lost more than 90 pounds (40.8 Kg.) within a few weeks. Attacks of acute cardiac decompensation with cyanosis occurred. Dextrose was given intravenously a number of times, and a digitalis preparation was given regularly. Morphine had to be given continuously in doses of 2 grains (0.13 Gm.) a day but did not control the delirium. The large doses had to be kept up for several weeks after the delirium.

Vomiting occurred at intervals during the delirium. Near the close of it, at one time there was a large amount of sugar in the urine with a trace of diacetic acid.

Hunger was marked for about ten days following the delirium, when the patient was given double portions of food. The intake of fluid averaged 4,000 cc a day.

During this time, cramps were first complained of with some distention in the upper part of the abdomen, and peristaltic waves were noticed. For a period of ten days, there were diarrhea and persistent vomiting. On July 2, a roentgen-

ologic examination proved the condition to be a marked duodenal obstruction. Medical management with small frequent feedings and changes of position, including elevation of the pelvis, was instituted. An attempt was made to pass a duodenal tube, but the patient refused.

For about a month, there was no vomiting, but the colicky pains and visible duodenal dilatation persisted after the intake of all fluids. During this period, acute decompensation of the heart recurred for a few days with edema over the dependent portions of the body and an enlarged liver. This condition improved, but two days after again starting the administration of compound solution of iodine there were diarrhea and vomiting of 1,200 cc which occurred every other day for six days. The dilated duodenum was visibly larger, and the peristalsis was more marked, passing chiefly from right to left. At the end of eight days, the patient had lost 19 pounds (8.6 Kg), but his heart and hyperthyroidism

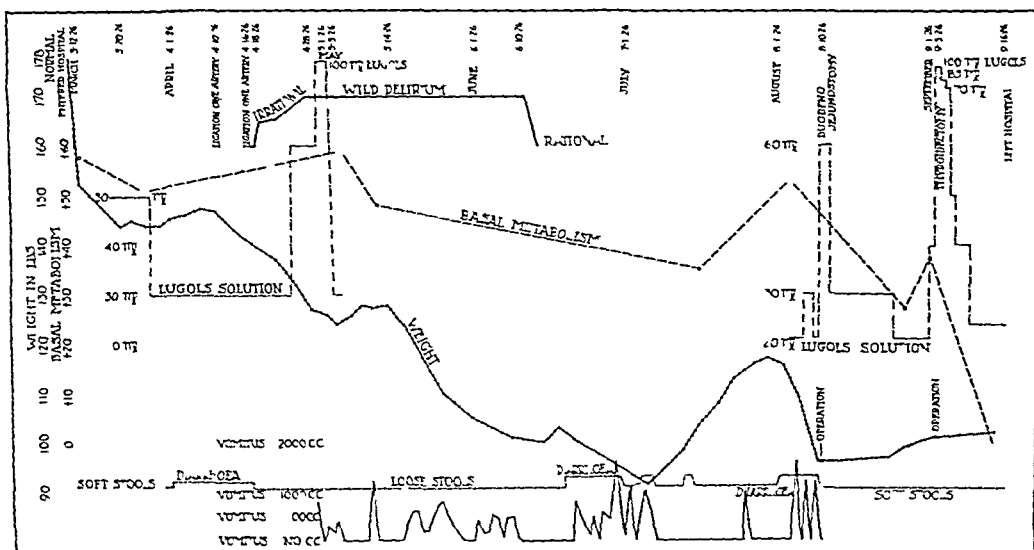


Fig 1 (case 1)—The clinical course of chronic idiopathic duodenal ileus, developing during acute hyperthyroidism

seemed improved. A similar temporary clinical improvement, especially of the condition of the heart, was noted previously on a number of occasions which were associated with loss of weight and dehydration.

At this time the patient was in a desperate condition from the duodenal obstruction, and a duodenojejunostomy was decided on.

**Laboratory Examination**—The basal metabolism rate was plus 57 at the time of entrance. It remained high until after the duodenojejunostomy, when there was a slight fall with a subsequent rise. After thyroidectomy three weeks later, it dropped to normal.

The urine showed a trace of sugar at the time of admission. During the delirium there were intermittently a trace of albumin and a few casts. At one time, near the end of delirium (June 6) there was a large amount of sugar with some diacetic acid. During the last month when dilatation of the duodenum was visible daily the urine was normal with the exception of an occasional trace of albumin with a few casts.

The Warrington reaction of the blood was negative.

When the patient was admitted to the hospital, the hemoglobin was 98 per cent and the white blood count was 7,400. The blood pressure was 124 systolic and 76 diastolic. After two months of delirium with a loss of one-half the body weight there was a little drop in the hemoglobin and number of red blood cells. On May 6, a test showed no hemolysis or agglutination of erythrocytes in various dilutions of a physiologic solution of sodium chloride with a 6 per cent dextrose solution. The blood calcium on June 7, late in the delirium, was 13.55 mg. On June 7, while the patient was delirious and critically ill, the carbon dioxide volume was 51.3 per cent and the blood sugar was 106.6 mg. per hundred cubic centimeters. On June 28, during the symptoms of marked dilatation of the duodenum, the carbon dioxide volume was 56 per cent.

On July 2, during the time of almost complete obstruction of the duodenum, as shown by the x-rays, the urea nitrogen was found to be 36.68 and the blood chlorides 445 mg.

The stools were yellow or brown and were usually soft and mushy, but watery at times. Occult blood was usually absent.

*Roentgenologic Examination*—On July 2, after ten days of severe obstructive symptoms (fig 2), the patient was weak and could not stand. He did not take a full mug of barium sulphate. There was considerable fluid in the stomach, which was large and dilated. Peristalsis was rather slow during the time of observation. Definite peristaltic waves were seen closing off the end of the antrum. By turning the patient a little on one side, the barium passed through the pylorus and filled the duodenum, which was distended from three to four times the normal size. There seemed to be a good cap. After several minutes, and on turning the patient to the left side, a trace of barium was seen in the small bowel beyond the duodenum. The patient was so weak that further observations could not be made. The roentgenograms at this time showed a large dilated stomach, a patent dilated pylorus, a fair duodenal cap and extremely large dilated second and third portions of the duodenum. The point of obstruction as determined from the fluoroscopic examination and the roentgenograms was apparently near the duodenojejunal flexure, but owing to the lack of filling of the terminal duodenum over the vertebra, the actual point of obstruction could not be determined. The pylorus was situated over the third lumbar vertebra, and the duodenojejunal flexure was somewhat to its left.

*Duodenojejunostomy*—On Aug 10, 1926, with the patient under ethylene anesthesia, a duodenojejunostomy was done. The abdomen was opened to the right of the midline. The transverse colon was lifted up, and the duodenojejunal flexure appeared to lie near the vertebra. The jejunum, which was of normal size, turned and extended downward directly into the pelvis. The remainder of the small intestine was entirely in the true pelvis. A loop of jejunum was brought up to the transverse infracolic portion of the duodenum, where a lateral anastomosis was made. Silk was used for the outer layer and catgut for the inner layer of sutures. No clamps were used. Considerable retroperitoneal fat was present in spite of the marked emaciation. The duodenum was empty and did not appear to be greatly enlarged. Several stitches were taken at each end of the union to prevent angulation of the jejunum.

Following the duodenojejunostomy the obstructive symptoms were permanently relieved, and food was taken without further distress. No more peristaltic waves were seen. Compound solution of iodine was given. A subtotal thyroidectomy was done twenty-four days later.

*Thyroidectomy*—On Sept 3, 1926 with the patient under ethylene anesthesia, a subtotal resection of both lobes of a large thyroid and isthmus was done. The parathyroids were unusually plainly visible and were avoided. A crisis was passed at the thirtieth hour with a temperature of 104.4 F. Convalescence was then uneventful.

*Pathologic Changes of the Thyroid Gland* The specimen consisted of two large portions which weighed 140 Gm. They were moderately firm and had

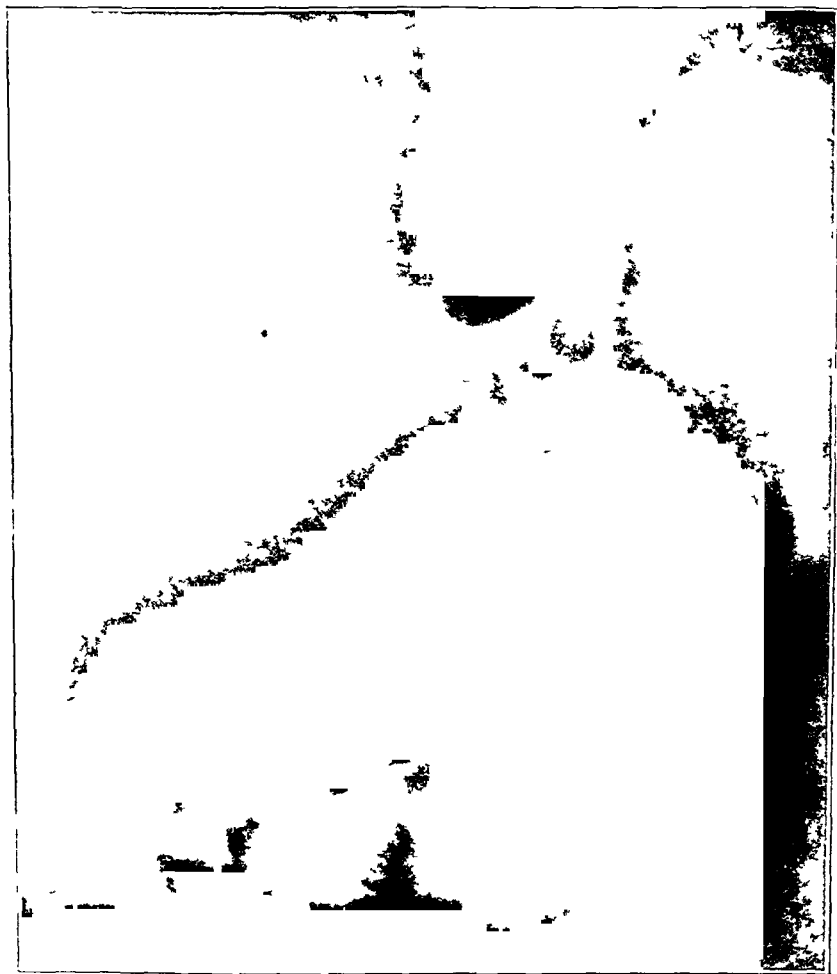


Fig 2—Roentgenogram of the markedly dilated duodenum and stomach, in the horizontal position, after ten days of acute obstructive symptoms

several nodules of increased consistency. There were several encapsulated, round cystlike areas filled with gray glistening mucoid material. The largest of these was 1 cm in diameter. The stroma was gray and rather fibrous. The microscopic examination showed hyperplasia and hypertrophy.

*Course*—Two months after operation the patient had gained 80 pounds (36.3 Kg.) in weight and there were no complaints. At this time a fluoroscopic



examination was made and roentgenograms were taken. There was no evident dilatation of either the stomach or the duodenum, which emptied barium readily through the duodenojejunostomy stoma. When the patient was lying down, some of the barium passed out normally through the terminal duodenum, which was nearly horizontal (fig 3). The third and fourth portions of the duodenum had considerable mobility to the left. When the patient was standing, the terminal duodenum appeared almost vertical with the formation of an acute angle in the jejunum, which may have been the result of the duodenojejunal anastomosis. The terminal duodenum was at the level of the upper edge of the fourth lumbar vertebra. The pylorus was about the same level, but appeared slightly higher in the recumbent position.



Fig 3—Roentgenogram taken two months after duodenojejunostomy, in the horizontal position. Complete relief from symptoms. The normal appearing duodenum emptied partly through the newly formed stoma and partly through the terminal segment with no evidence of obstruction.

About four months after operation, the patient suffered a severe mental shock from a business reverse and was acutely depressed. He developed auricular fibrillation and tachycardia for several days. One month later, he started a new kind of work, apparently feeling physically well. Two weeks later, he was found dead from drowning.

*Postmortem Report*—The anatomic diagnosis was marked vesicular emphysema (asphyxiation from drowning), hyperplastic and hypertrophic parenchymatous thyroid, both lobes partially removed, persistent lymphoid tissue of the thymus, slight chronic fibrous myocarditis, chronic diffuse nephritis, secondarily

contracted kidneys, moderate hyperplasia of the spleen, fatty changes of the aortic lining, fibrous adhesions between the anterior abdominal wall and the great omentum, lateral anastomosis between the duodenum and the jejunum, long since absent gallbladder and appendix vermiformis, and right fibrous pleuritis.

The body measured 185.5 cm in length. A loop of jejunum crossed the front of the spine horizontally just behind the transverse colon. The weight (estimated) of the liver was 1,500 Gm, and the edges were sharp. The borders of the spleen were sharp, it measured 12 by 15 by 8 cm.

The weight (estimated) of the kidneys was 300 Gm. They had a free capsule and the surface was slightly uneven, suggestive of a "granular" kidney. On section, the cortex of the left kidney was from 4 to 6 mm, the right, from 6 to 7 mm. The cortical markings were fairly well defined. The medulla was light purple and definitely opaque. The pelvic fat was plentiful and the pelvic mucosa unaltered.

The thyroid consisted of a zone from 1.5 to 1.8 wide on the right side and 1.6 on the left. It was grayish brown and the colloid was clearly visible. Attached on the left side lower down, there was an additional encapsulated mass of thyroid 2.5 cm in diameter, translucent and gelatinous.

The stomach contained 60 cc of watery fluid. The pyloric ring was 3.3 cm in circumference.

The heart was 16 by 12 by 8.5 cm and weighed (estimated) 450 Gm. The right side was convex. The myocardium was opaque and brownish gray. The width of the left ventricular wall was 1.5 cm and that of the right, from 1 to 3 mm. The mitral orifice was approximately 1.3 cm in circumference, the aortic 0.97, the pulmonary 0.97 and the tricuspid 1.5 cm. The depth of the left ventricle was 11.5 cm. The left coronary artery was 1 cm in circumference, the left descending 0.7 and the right 0.7 cm.

**Microscopic Examination.** Sections of the thymus contained an abundance of lymphoid tissue and many Hassall's corpuscles. Only at the periphery of the section was there slight replacement of the lymphoid tissue by fat.

In sections of the thyroid there were fields of connective tissue with scattered acini, near the periphery of the gland, elsewhere the tissue was practically all glandular, being made up of small and large acini containing a uniformly stained pale and purple material. The epithelium was in places cuboidal, elsewhere columnar and the latter formed papillae-like infoldings into the lumen of the acini. In the fields of columnar epithelium there were collections of round cells.

In the myocardium there was some connective tissue increase in the intermuscular spaces. A few of the small capillaries were filled with polymorphonuclear leukocytes and red blood cells and some had a perivascular round cell infiltration. The muscle fibers were extensively fragmented. The liver had some thickening of its capsule by connective tissue which was infiltrated with round cells. There was a rather marked infiltration of round cells in the portal spaces. Changes in the parenchymal cells were negligible.

The capsule of the kidney was thickened and in the cortex were many collections of round cells and strands of connective tissue traversing the entire cortex. The epithelium was swollen and the cytoplasm granular. The glomerular tufts were engorged with blood and the capsule unchanged.

The evidence pointed to the fact that death was due to drowning. To what extent natural causes contributed could only be speculated. The heart, thyroid and kidneys, however, all showed morbid changes and those in the heart were sufficient to cause heart failure under sudden exertion.

The anatomic studies of the specimen of duodenum and related structures were made (fig 4) by me. The duodenum was empty and corresponded to the circular type with no definite angles, but the horizontal, descending, transverse and ascending portions could be identified. The wall was apparently of normal thickness.

The circumference of the duodenum was 4.5 cm in the first portion, while the second portion was slightly enlarged and measured 8 cm at the level of the ampulla of Vater, and 7 cm proximal to the duodenojejunosomy stoma which measured 15 cm long by 1 cm wide. At one end there was a silk suture but no evidence of ulcer.

The root of the mesentery broadened out in a triangular shape to measure 4 cm broad at its crossing over the duodenum, with the artery and vein lying near

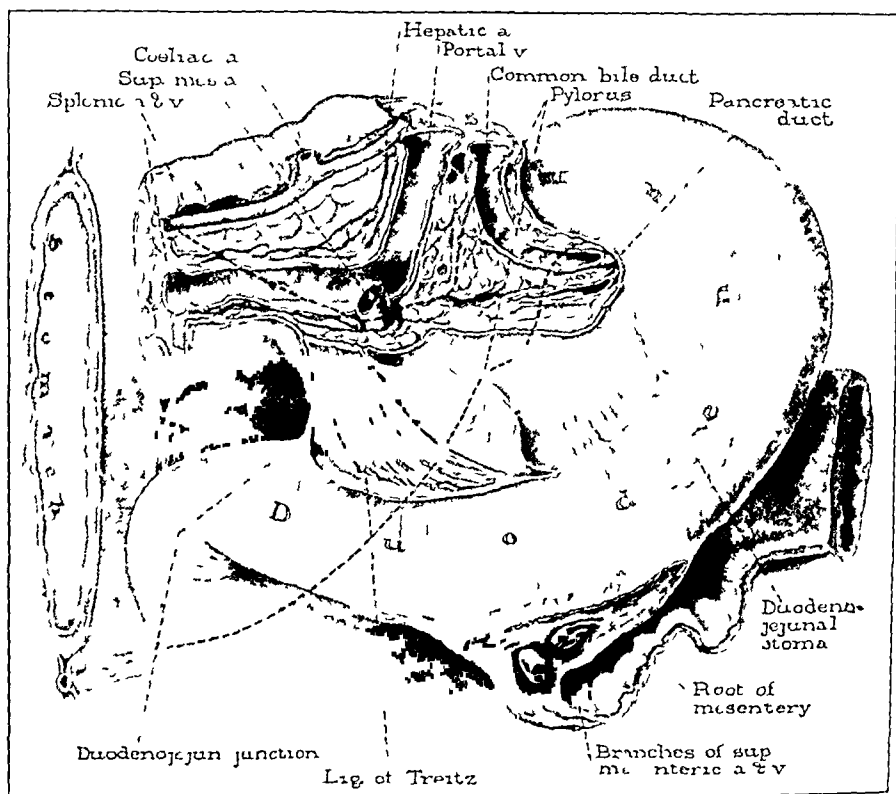


Fig 4—Drawing of the duodenum and adjacent viscera, removed at necropsy, viewed posteriorly. A slight dilatation of the descending portion and none of the remainder of the duodenum could be demonstrated. There was a slight definite narrowing of the duodenum beneath the blood vessels in the mesentery, but none at the duodenojejunal flexure.

the middle. The circumference of the duodenum for about 2 cm beneath the root of the mesentery was narrowed down to 4.8 cm, while proximally it was 6.5 cm, and distally, 5.2 cm. Here, the duodenal mucosa was flattened out and adherent, while it was redundant, both proximally and distally. The narrowed segment beneath the mesentery was apparently the site of the former obstruction.

The terminal end of the duodenum beyond the mesentery measured 6 cm in circumference, with no evidence of kinking. The jejunum was larger and measured 7.8 cm in circumference below the stoma.

The distance from the pylorus to the ampulla of Vater measured 12 cm, to the duodenojejunal anastomosis 20 cm, to the right side of the root of the mesentery of the small intestine 24 cm, to the crossing of the superior mesenteric artery 27 cm and to the duodenojejunal juncture 31 cm

The muscle fibers of the ligament of Treitz passed as a band 15 cm wide slightly to the left of the superior mesenteric artery and directly downward on its left side to insert on the duodenum. They inserted 55 cm along the duodenum, extending 15 cm to the right of the superior mesenteric artery. By gentle traction on the artery I could produce a constriction of the duodenum beneath it. Beneath the artery separating it from the duodenum there was only a 2 mm layer of fat, while it was 5 mm thick in the mesentery above. It is probable that counter pressure posteriorly from the bodies of the vertebrae or aorta and from a wide ligament of Treitz above aided obstruction.

The common bile duct was slightly dilated above its outlet. The largest circumference measured 2 cm. The pancreatic duct joined the common duct within the duodenal wall. The ampulla was small and could not be easily probed.

The jejunal flexure was several centimeters distal to the duodenojejunal junction, perhaps due to the transverse position of the jejunum from the anastomosis. There was no evidence of any obstruction, narrowing or angulation at this flexure, even with considerable downward traction on the jejunum.

The microscopic examination of the duodenum showed no pathologic changes. There was no evident hypertrophy of the wall proximal to the crossing of the mesentery as compared to that segment under it and that, distally. The outer muscle layer remained constant in width while the inner circular muscle layer was increased slightly in width, respectively, from above downward.

The duodenum, which had been partially split open, was carefully sutured and distended with barium.

Roentgenograms showed a fairly well filled duodenum, except for the first portion which was somewhat distorted, due to postmortem shrinking. The descending portion was the largest. There was some narrowing evident at the mesenteric root. The duodenojejunal flexure was well distended and appeared to offer no opportunity for stasis at this time. The flexure was seen to be definitely in the jejunum, and beyond the terminal fixed point of the duodenum.

Two other cases of hyperthyroidism showed mild duodenal stasis, one associated with high grade stomach retention.

**CASE 2—History**—F W A, a man aged 62, complained of weakness, loss of appetite, loss of 47 pounds (21.3 Kg) in weight and a vague abdominal distress with considerable colicky pains and constipation. The abdominal distress was present the last five weeks and he had eaten and drunk little since then. The diagnosis was primary exophthalmic goiter with mild duodenal stasis.

**Examination**—The roentgenologic examination of the stomach showed a rather persistent stasis with considerable dilatation of the second portion of the duodenum. The basal metabolic rate was plus 44. The patient was given compound solution of iodine and medical treatment with relief from abdominal symptoms. The superior thyroid arteries were ligated and two months later a subtotal thyroidectomy was done. Ten days later, on fluoroscopic examination there was observed prompt filling of the duodenum with a slight delay in the second portion. An occasional rush peristalsis carried the barium into the jejunum alternating

with moderate reverse peristalsis. Three months later, the patient had gained 35 pounds (159 Kg) and had no complaints. The patient was well on examination one year later.

**CASE 3—History**—A D, a woman, aged 40, had a condition which was diagnosed as gastric and duodenal stasis with adenomas of the thyroid gland and mild hyperthyroidism. An attack of abdominal pain without vomiting had occurred one day previously. Recent less severe similar attacks were usually associated with constipation. A goiter with several palpable adenomas had been observed one year previously. She had been under medical care ever since. There was a history of spastic colitis.

**Examination**—Roentgenologic examination of the colon gave negative results except for a moderate spasm in the descending and sigmoid portions. The stomach filled readily, with good peristaltic waves which closed off completely to the end of the antrum. The pylorus was slow in opening, and then the duodenal cap filled well. There was some stasis in the second portion of the duodenum and reverse peristalsis. Four hours later, three fourths, and twenty-four hours later, one half, of the barium was still in the stomach. At these times the duodenal cap was filled, but the remaining portion of the duodenum was empty.

The basal metabolic rate was plus 13. The patient was treated by medical management for the abdominal distress with gradual improvement. One month later fluoroscopic examination of the stomach showed slightly delayed emptying with moderate reverse peristalsis in the second portion of the duodenum. One-half hour later the stomach was half empty and the duodenum was emptying normally into the small intestine. The abdominal symptoms were apparently largely relieved by medical management, and no acute exacerbations were noted in the subsequent year.

I have made roentgenologic examinations in several other cases of acute hyperthyroidism in which the patients have persistently vomited or have had abdominal pains. In these cases there was no evidence of duodenal or gastric dilatation or obstruction. The entire colon was spastic in a few cases.

Only two cases are classified in the literature as chronic duodenal ileus in which hyperthyroidism was noted. Neither case, however, may be considered one of classic duodenal ileus. Wilkie<sup>1</sup> reported a case of exophthalmic goiter with persistent bilious vomiting for three months. The roentgenograms showed calcareous tuberculous glands in the root of the mesentery, which it was thought contributed to the obstruction. The duodenal dilatation had not been great, and the observer thought that the duodenojejunostomy which he had done was probably not indicated and possibly had aggravated the thyrotoxicosis, since the patient died of a subsequent thyroidectomy while still in the hospital.

Higgins<sup>2</sup> reported one case with recent hyperthyroidism showing obstructive symptoms over several years. There was no vomiting, but nausea and regurgitation with loss of 20 pounds (9 Kg) of weight.

1 Wilkie, D P D. Chronic Duodenal Ileus, *Am J M Sc* **173** 643 (May) 1927, *Brit J Surg* **9** 204, 1921.

2 Higgins, C C. Chronic Duodenal Ileus, *Arch Surg* **13** 1 (July) 1926.

during the preceding year. There was gastroparesis and marked dilatation of the duodenum. Following thyroidectomy, the dilatation of the duodenum improved with the patient under medical treatment. Higgins reported four cases of duodenal ileus in which the patients had nontoxic goiters. Two of these were relieved by a duodenojejunostomy and two with medical treatment, but the dilatation was not great. In Wilkie's case the vomiting may have been due to the hyperthyroidism, rather than to the obstruction of the duodenum.

#### GENERAL CHARACTERISTICS

*Etiology*—Chronic idiopathic duodenal ileus is more common in women. The most characteristic point of obstruction usually occurs at the crossing of the superior mesenteric artery in the root of the mesentery of the small intestine although obstruction may occur at any point on the duodenum. The true idiopathic type is characterized by the inability to determine any pathologic cause, even at postmortem examination.

Congenital abnormalities and acquired intrinsic or extrinsic pathologic changes of the duodenum are fairly common and clinically it is difficult to differentiate a pathologic from an idiopathic obstruction.

Congenital atresia, or compression of the lumen by anomalous bands or blood vessels may occur in any part of the duodenum. Jackson<sup>3</sup> reported a case of partial obstruction in the second part due to a remnant of the anterior mesogastrium. Devine<sup>4</sup> reported the occurrence of megaloduodenum in children. Bakay<sup>5</sup> reported a case of obstruction by a Treitz hernia. The Kelloggs<sup>6</sup> mentioned obstruction due to hypertrophy of the valvulae of Ochsner's muscle, from inflammation and new growths.

There are numerous reports of cases of extrinsic pathologic changes producing obstruction. Postoperative obstruction has been observed due to a kinking of the duodenojejunal angle (Brown et al.<sup>7</sup>) or a localized peritonitis (Duval<sup>8</sup>) following gastrojejunostomy.

3 Jackson, R. H. Congenital Constriction of the Duodenum Due to an Abnormal Fold of the Anterior Mesogastrium. *Ann Surg* **84** 723 (Nov.) 1926.

4 Devine, H. B. Basic Principles and Supreme Difficulties in Gastric Surgery. *Surg Gynec Obst* **40** 1 (Jan.) 1925.

5 Bakay, L. V. Disturbances of Passage in the Duodenum. *Arch f Klin Chir* **141** 135 (May 22) 1926.

6 Kellogg, E. L. and Kellogg, W. A. Chronic Duodenal Stasis. *Radiology* **9** 23 (July) 1927.

7 Brown, G. E., Eustermann, G. B., Hartman, R. H. and Rowntree, L. G. Toxic Nephritis in Pyloric and Duodenal Obstruction. Renal Insufficiency Complicating Gastric Tetany. *Arch Int Med* **32** 425 (Sept.) 1923.

8 Duval, P., Roux, J. C., Gatellier and Montier. Relations entre lésion infectieuse des parois gastriques et certains troubles consécutifs à la gastro-entérostomie. *Bull et mem Soc nat de chir* **52** 270 1926.

There are two chief theories in the production of the idiopathic type of obstruction in the terminal duodenum, the mechanical and the neuromuscular. The mechanical type of marked idiopathic obstruction with hyperperistalsis is an unusual condition. Undoubtedly, fewer cases would be so classified if postmortem studies were made. Hyperperistalsis may be observed under the fluoroscope, and occasionally it is visible after the intake of fluids. This is the characteristic chronic type of duodenal ileus, but cases with a pathologic basis for duodenal stasis are reported under this classification.

The most commonly accepted belief is that obstruction of the terminal duodenum is due to pressure from the superior mesenteric artery.

At operation, Devine observed that the dilatation stops at the point of crossing of the superior mesenteric artery. Wilkie relieved the dilatation by lifting up the drag on the root of the mesentery.

Halpert<sup>9</sup> stated the belief that acute and chronic duodenal obstruction have the same etiology. In a study of the anatomy, he has concluded that pressure is caused by traction due to displacement of the small intestine into the pelvis, and that while jejunal branches of the superior mesenteric artery lie between the leaves of the mesenteric fold, they do not cause the obstruction. He located the point of obstruction on the pars horizontalis inferior just proximal to the ascending portion and some distance from the duodenojejunal flexure.

He found that the angle between the superior mesenteric artery and the aorta was at the level of the first lumbar vertebra, whereas the part of the duodenum at which obstruction occurs was at the level of the third lumbar. He found that the left renal vein may be compressed in this angle beneath the artery but never the duodenum. Clinically, he differentiated a primary arteriomesenteric occlusion followed by paralysis and passive dilatation of the stomach and a secondary dilatation of the duodenum following that of the stomach.

The relation of the origin of the root of the mesentery either to the right or to the left of the lumbar vertebra may influence obstruction. Snitzler<sup>10</sup> believed that obstruction was more likely when the ligament was attached to the right of the median line. Case<sup>11</sup> observed in the supine position that pressure of the vertebrae against the normal duodenum will sometimes cause obstruction at the "duodenojejunal flexure," with writhing duodenal movements. He also observed that if the

9 Halpert, B. The Arteriomesenteric Occlusion of the Duodenum. An Anatomical Study, *Bull. Johns Hopkins Hosp.* **38** 409, 1926, *Virchows Arch. f. path. Anat.* **244** 439, 1923.

10 Snitzler, quoted by Staveland. *Surg. Gynec. Obst.* **11** 288, 1910.

11 Case, James T. Chronic Obstruction of the Small Intestine, *Bull. Battle Creek Sanit. & Hosp. Clinic* **22** 193 (Sept.) 1927, *Radiology* **9** 1, 1927.

patient had been resting on his right side preceding the roentgenologic examination, the duodenum was usually more than normally distended.

The development of the duodenum is separate from the small intestine as described by Hunter<sup>12</sup>. He observed, first, the formation of two loops in the straight duodenum, second, the rotation of the colon and changes in the adjacent viscera and, finally, the disappearance of the mesentery with the duodenum assuming its retroperitoneal position. The loop is formed before the development of the pancreas and is not molded by it.

Dwight<sup>13</sup> in a study of adult types of duodenum found that the primitive form is ring-shaped from which all others arise and on relaxation it tends to resume this shape. On distention he found the U- and V-shapes most common, others were C-shaped or indeterminate. The superior flexure was usually at the level of the first lumbar vertebra and the lowest point of the descending portion decidedly lower than usually reported, usually opposite the fourth lumbar. The statement that usually the third portion crosses the aorta presumably with no peritoneum intervening and that the fourth portion ascends on its left, he found incorrect. He observed in fifty-four instances that the third portion crossed the aorta only eleven times, the fourth portion crossed it thirty-seven times, and the duodenum was entirely on its right side six times. In many cases in which the duodenum lay in front and in some to the left of the aorta, a fold of peritoneum lay between. It was difficult for Dwight to determine whether the original attachment of the mesentery was at the right or left of the aorta, but he believed it was along the right with intervening peritoneum frequently present. Halpert stated that the muscle of Treitz holds the terminal duodenum in position. However, Jonnesco<sup>14</sup> admitted that the fourth part slides easily and is less firmly attached than the second or third parts. Abnormal fixation of the terminal part has been suggested as the cause of obstruction.

Dwight found that the first part of the duodenum in man was egg-shaped and smooth and that the other parts presented irregular folds especially the second. The largest circumference was usually in the second or third part. In two cases it was abnormally large, measuring 18 cm. in the second part.

The duodenum has been divided by Huntington<sup>15</sup> into a supramesocolic and an inframesocolic part by the root of the mesocolon. The

12 Hunter, R. H. Development of the Duodenum. *J. Anat.* **61** 205 (1917) 1927.

13 Dwight, T. Notes on the Duodenum and the Pylorus. *J. Anat. & Physiol.* **11** 517 1897.

14 Jonnesco quoted by Dwight (footnote 13).

15 Huntington, G. S. The Anatomy of the Human Peritoneum and Abdominal Cavity. Philadelphia: Lea Brothers & Company, 1903.



inframesocolic part is further divided by the root of the mesentery of the small intestine into the pars inframesocolica dextra and sinistra

Obstruction of the terminal duodenum by prolapse of a part or all of the colon has been described Bloodgood,<sup>16</sup> however, believed that the prolapsed cecum pulled on the mesentery of the small intestine and that duodenal obstruction resulted when the last portion of the ileum had a short mesentery He obtained relief in a few cases by resection of the right half of the colon Traction of the cecum or ascending colon on the mesocolon may also press on the second part of the duodenum (Quain,<sup>17</sup> Duval, Kellogg and Kellogg) forming an arteriomesocolic type which must be differentiated from the arteriomesenteric type of terminal duodenal obstruction

The Kelloggs have mentioned traction on the superior mesenteric artery by the pull of the prolapsed cecum on the ileocolic artery They found that the prolapse of the transverse colon may also cause compression when the colic artery is given off above the duodenum or by a pull on the superior mesenteric artery itself Wilkie, Duval and Gregoire<sup>18</sup> reported a case of obstruction by a right colic artery crossing the duodenum vertically The Kelloggs observed obstruction due to an arterial anastomosing branch between the right colic and the middle colic arteries

Duodenal obstruction by prolapse of the stomach has been described The Kelloggs stated the belief that gastropotosis increases the acuteness of the superior duodenal flexure and that obstruction may occur either at the inferior duodenal flexure, the mesenteric root or at the duodenojejunal flexure Bakay described compression of the duodenum by the lesser omentum in gastropotosis De Luna<sup>19</sup> observed obstruction in the first and second portion in gastric ptosis Adams<sup>20</sup> stated that a kink usually occurred at the duodenojejunal flexure but occasionally at the junction of the first and second parts of the duodenum He believed that a duodenojejunal kink is due to the drag of a ptosed stomach on the first part of the duodenum, which pulls it around the head of the pancreas until it is held at the duodenojejunal angle

Recently the Kelloggs have reported compression of the jejunum at the pelvic brim by prolapse of the small intestine into the pelvis as a new cause of duodenal stasis

16 Bloodgood Dilatation of the Duodenum in Relation to Surgery of the Stomach and Colon, *J A M A* **59** 117 (July 13) 1912

17 Quain, E P Periduodenitis, *Minnesota Med* **9** 431 (Aug) 1926, *Am J Surg* **38** 198, 1924, Pathogenic Ptosis of Right Colon, *Arch Surg* **6** 638 (April) 1923

18 Gregoire, quoted by Wilkie (footnote 1)

19 De Luna, C Le syndrome duodenal dans la ptose gastrique, *Marseilles med* **63** 1261 (Aug 15) 1926

20 Adams, J E Duodenal Ileus *Brit J Surg* **14** 67 (July) 1926

Ptosis of the right kidney tumors pressure from the pancreas, aneurysm and infection in the gastric wall and perigastric lymphatics (Duval) may be factors in duodenal obstruction

The neuromuscular type of duodenal obstruction may occur either from increased contraction or from paralysis of the duodenal musculature This theory is advocated by Robertson and Devine who question the mechanical theory because of failure to relieve the symptoms in a number of cases by short circuiting operations Some failures have been reported by others However, in the absence of a thorough anatomic or postmortem study, any comparison of medical and surgical treatment in the varied types of stasis classified as chronic duodenal ileus is unreliable Robertson<sup>21</sup> believed that the obstruction is due to a disturbance of nerve balance between the vagi and the sympathetic He stated that either stimulation of the sympathetic or a depression of the vagi may result in dilatation Devine stated that the sympathetic tonus aids retention in the stomach and duodenum The function of the parasympathetic is to empty the viscus and it acts intermittently, the two systems being complementary He considered duodenal ileus as an exaggerated retention similar to cardiac spasm due to neuromuscular derangement above the duodenal rudimentary sphincter Alvarez<sup>22</sup> experimentally found that both the vagus and splanchnic nerves serve as inhibitors and regulators of intestinal activity The only sign of antagonism was found in conduction, which was improved by vagotomy and injured by splanchnicotomy

Carlson,<sup>23</sup> Bolton and Salmond<sup>24</sup> considered antiperistalsis of the duodenum as a normal condition for the purpose of mixing food with the digestive juices Glenard<sup>25</sup> believed that physiologic retention in the duodenum was produced by pressure on the duodenum by the mesenteric ligament

The action of morphine and opium on the duodenum and intestinal tract is of interest in my case because of the large continued doses given

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21 Robertson G Acute Dilatation of Stomach and Intestinal Tube with Consideration of Chronic Duodenal Ileus *Surg Gynec Obst* **40** 206 (Feb) 1925

22 Alvarez, W C The Effects of Degenerative Section of the Vagus and the Splanchnic Nerves on the Digestive Tract, *Proc of the Staff Meetings of the Mayo Clinic* **4** 205 (Jul 3) 1929

23 Carlson A J Movements of the Alimentary Tract in Experimental Animals *Illinois M J* **55** 429 (June) 1929

24 Bolton C, and Salmond R W A Antiperistalsis of Duodenum and Its Relation to Pyloric Regurgitation *Lancet* **1** 1230 (June 11) 1927 Salmond Observations on the Movements of the Duodenal Contents with Special Reference to Antiperistalsis and Pyloric Regurgitation *Proc Roy Soc Med* **21** 1361 (June) 1928

25 Glenard quoted by Staveland (footnote 31)

during the persistent delirium and during the onset of the ileus Weitz and Vollers<sup>26</sup> found that opium increases the tonus of the stomach and intestines There was an increase of the pendulum movements of the intestine, which they thought might favor the resorption of fluids and account for the constipating action of the opium Recently I studied roentgenologically the case of a man, aged 44, who had been a morphine addict for ten years The stomach was normal The duodenum filled well and emptied normally, but there was occasional antiperistalsis with slight puddling The colon was normal except for a moderate spastic condition throughout

Hypertonicity may have been a factor in the duodenal obstruction in my case and also in the diarrhea which occurred with each aggravation of duodenal obstruction However, the administration of morphine and opium was discontinued before the last and worst attack of obstruction Hypertonicity might have initiated an obstruction which easily became a mechanical, valvelike, obstructing angulation of the duodenum at the crossing of the mesentery Higgins stated that hyperperistalsis was present in marked cases of duodenal ileus which required short circuiting operations

*Pathologic Changes*—The anatomic changes reported previously in chronic idiopathic duodenal ileus have been limited apparently to observations under the roentgen ray and at operation At operation, Wilkie frequently observed a bulging of the first part of the duodenum with the stomach dilated and the pylorus patent On lifting up the transverse colon, he observed that the small intestine was usually in the pelvis and that the third part of the duodenum was usually dilated Others have reported dilatation up to the point of crossing the superior mesenteric artery

A plastic exudate about the superior duodenojejunal fossa has been described by Miller<sup>27</sup> and must be differentiated from the changes such as may occur in a localized peritonitis following a gastrojejunostomy or associated with a gastric ulcer Wilkie stated that there was usually a lack of hypertrophy of the muscle wall in chronic duodenal ileus but that it might occur Devine rarely found evidence of it The Kelloggs stated that there was first hypertrophy and hyperperistalsis with late atrophy, dilatation and stasis They noted that the pylorus was at first hypertrophied and spastic, later becoming incompetent

26 Weitz, W, and Vollers, W Ueber die Beeinflussung der Bewegungen des Magens und Darms durch Opium, Ztschr f d ges exper Med 54 161 (Jan 25) 1927

27 Miller E M, and Brown, R C Chronic Duodenal Ileus, S Clin North America 5 1117 (Aug) 1925

From roentgenographic examinations, the Kelloggs have described four types of duodenal stasis

1 The asthenic duodenum in which symptoms were latent or toxic. Roentgen examination showed delay or puddling in the duodenum, with sluggish peristalsis and slight or no dilatation.

2 Duodenal obstruction with an incompetent pylorus. The dilatation of the stomach was moderate or absent. The roentgenologic examination of the duodenum gave negative results or occasionally showed reverse peristalsis.

3 Duodenal obstruction with hypertrophy. The duodenum was elongated and its walls were thickened. Under the fluoroscope it was seen to labor over its contents (writhing duodenum). Cramplike pains were common.

4 A dilated duodenum. The area of tympany was increased and pain was steady or cramplike. This type was most readily demonstrated by the roentgen examination.

There was practically complete obstruction in my first case under the fluoroscope, but there was a slight passage of barium on turning the patient to the left side and in the prone position. This together with hyperperistalsis would speak for a mechanical nonstrangulating type of obstruction.

The duodenal stasis in my other cases was of a mild type, in case 2 reverse peristalsis was still observed after thyroidectomy.

Experimentally, Berg et al.<sup>28</sup> have produced a persistent duodenal obstruction in dogs which should not be compared to the clinical idiopathic ileus because the latter may act intermittently. These authors obtained a dilatation and hypertrophy above the obstruction with emaciation, but there were no symptoms of intoxication. They usually found bacteria present. After partial obstruction bacteria especially of the colon group increased but later they occasionally decreased. Usually fewer organisms were found below the obstruction.

The anatomic type predisposing to duodenal obstruction has been described as spare and slender having a narrow costal angle and a broad pelvis.

*Associated Pathologic Processes*—Associated ulcers of the stomach and duodenum have been reported (Ryle<sup>29</sup>). Wilkie believed that the duodenal obstruction predisposed to ulcers. He found among seventy-five cases, four patients with gastric ulcers and three with both gastric and duodenal ulcers.

In cases of pathologic duodenal and pyloric obstruction, especially cases in which tetanus resulted, toxic nephritis has been observed by

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28 Berg, Melenev and Jobling. Experimental Chronic Duodenal Obstruction. Technique and Physiology. Arch Surg **14** 752 and 770 (March) 1927.

29 Ryle, J. A. Case of Duodenal Ileus with Perforating Duodenal Ulcer. Guy's Hosp. Rep. **76** 162, 1926.

Brown and others Associated lesions of the pancreas and gallbladder, some with jaundice, have been reported. Hyperthyroidism may be associated.

*Symptoms*—Chronic duodenal ileus is usually remittent or intermittent. The clinical symptoms may be vague or characteristic. They may date back to childhood or appear in adult life, especially following an emaciating illness or childbirth.

Pain is the most distressing symptom. Wilkie found that it usually occurs one-half hour after meals. It may be at the left or the right of the umbilicus. Epigastric fulness and flatulence are common after meals.

Vomiting of large amounts is usually present but occurs periodically. Wilkie observed it lasting from one to two days about every four to five weeks. It may occur at certain periods each day, frequently several or even many hours after a meal. The fluid is usually bile colored. There is often a dread of eating.

Loss of weight during the acute attacks may be rapid, with alarming dehydration. There may be tetany-like manifestations. The attacks are often described as bilious. They are often associated with headache, malaise, depression and neuralgia.

Toxic symptoms somewhat similar to uremia and shock have been described, but I have not noted previous reports of changes in the blood chemistry in the idiopathic type. In extensive pathologic obstruction of the duodenum, examinations of the blood chemistry have shown (Brown and others) a low level of chlorides, a high level of blood urea and of creatine and a high carbon dioxide carrying capacity.

It is significant that no changes were observed in the blood chemistry in my case during the acute exacerbations with persistent vomiting and loss of weight.

In experimental partial duodenal obstruction by Berg and his co-workers, there was also an absence of intoxication even though it produced dilatation with hypertrophy. Clinically, in acute intestinal obstruction and ileus, McVicar and Weir<sup>30</sup> found severe toxemia with dehydration before the occurrence of disturbances in the blood. Changes in the blood chemistry should therefore speak for pathologic changes such as a high grade stenosis from new growth or adhesions. However, acute dehydration, vomiting and emaciation may be present in either idiopathic or pathologic obstruction.

On physical examination in duodenal obstruction, the patient is usually found to be thin and may be emaciated. Tenderness may be present near the umbilicus. Distention and fulness may be marked.

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30 McVicar and Weir. Nature and Treatment of the Toxemia of Intestinal Obstruction and Ileus. *J. A. M. A.* 92:887 (March 16) 1929.

The stomach may be low and dilated. The observation of a huge distended duodenum filling almost the entire abdomen and extending below and to the left of the normal location with visible peristaltic waves as in my case is apparently rare. Wilkie has described a definite tympanic swelling of the duodenum in one case as unusual.

Haye's procedure of pressure upward and backward may demonstrate gas gurgling through the duodenum. The Cash symptom of duodenal splashing or succussion was occasionally observed by Kellogg and rarely by Wilkie.

#### PROGNOSIS AND TREATMENT

The prognosis will depend on the recognition of the various factors involved in the idiopathic as well as in the pathologic obstruction with the institution of appropriate treatment. In a well developed obstruction of the terminal duodenum, with hyperperistalsis a duodenojejunostomy is usually indicated. However the latter may not give complete relief when there are pathologic changes or neuromuscular disturbances involving other portions of the gastro-intestinal tract.

Obstruction of the proximal duodenum by anomalous bands or adhesions should be excluded. Quain has obtained good results by means of a transmesocolic duodenojejunostomy. The bands may occasionally be divided, a gastrojejunostomy may also give relief although it usually does not when obstruction is in the terminal duodenum (Adams). Resection of the colon as performed by Bloodgood is rarely necessary for any type of duodenal obstruction.

In a study of the late results in fifty-seven cases classified as chronic duodenal ileus Wilkie found twenty-three patients cured, eleven improved, twelve still having slight symptoms and nine without relief. The last group included the cases of visceroptosis. He found the best results in cases with roentgenographic evidence of dilatation and no evidence of mechanical obstruction. In thirty cases in which the patients were treated by duodenojejunostomy alone the Kelloggs found eighteen free from symptoms and nine improved. There were two deaths in a total of seventy-seven patients treated by duodenojejunostomy alone or combined with other procedures.

A lateral anastomosis of a loop of jejunum to the second portion of the duodenum as suggested by Barker and performed by Staveland<sup>31</sup> is usually the operation of choice in obstruction near the terminal duodenum. The stomach and duodenum should be aspirated if necessary before operation. It is unnecessary to use a clamp on the duodenum or the jejunum.

<sup>31</sup> Staveland, A. L. Chronic Gastromesenteric Ileus. *Surg. Gynec. Obst.* **11** 288, 1910.

The usual technic for a lateral anastomosis is satisfactory. The use of an outer row of fine silk or linen sutures is advisable, with additional sutures to prevent angulation of the jejunum. Some other operative procedures may be indicated when duodenal ileus is associated with anatomic or pathologic conditions.

#### SUMMARY AND CONCLUSIONS

In case 1 the following observations were made:

- 1 The stomach and pylorus were dilated together with the duodenum, and there was hyperperistalsis with a churning back and forth in the duodenum before operation.

- 2 There was no unusual ptosis evident in the stomach or duodenum, except that resulting from dilatation.

- 3 There was a subsidence of duodenal dilatation after operation.

- 4 At postmortem examination, the descending and inferior portions of the duodenum were widest proximal to the root of the mesentery. There was a narrowed segment beneath the mesentery containing the superior mesenteric blood vessels.

- 5 The ampulla of Vater was apparently continent.

- 6 A pull on the mesentery itself did not seem to produce a narrowing of the duodenal lumen.

- 7 The superior mesenteric artery crossed the duodenum about 4 cm from the duodenojejunal junction. A downward pull on this artery easily produced obliteration of the duodenal lumen beneath it.

- 8 There was no evidence of hypertrophy of the duodenal wall either at operation or at postmortem examination.

- 9 The ligament of Treitz was broad at its insertion. This band might have hypertrophied and increased the fixation of the duodenum, or it might have aided counterpressure against the superior mesenteric artery.

- 10 It seemed impossible by downward or lateral traction on the jejunum, by pulling on the ligament of Treitz or by distention of the duodenum to produce any narrowing of the lumen or kinking at the duodenojejunal flexure.

Factors arising from acute hyperthyroidism that may have favored duodenal obstruction were a suddenly increased fluid intake, emaciation, rigidity and retraction of the abdominal muscles, irritable colon with diarrhea, constant lying on the right side, cardiac decompensation, a neuromuscular disturbance perhaps aggravated by large doses of morphine and opium and delirium.

A congenital origin, the standing position, inflammation of the gall-bladder and the presence of pathologic changes or anatomic anomalies

may be eliminated as factors in this case. Probably after a certain amount of distention, a mechanical valve forms under the root of the mesentery and in turn aggravates the contributing factors.

Marked hyperperistalsis may occur with a huge dilatation of the duodenum of several weeks' duration, and the lumen may return almost to its normal size shortly after duodenojejunostomy with little evident hypertrophy of the wall.

Chronic nephritis may result, but changes in blood chemistry such as observed with marked pathologic obstruction or stenosis of the duodenum do not necessarily occur. Severe hyperthyroidism may not act directly in the causation of duodenal obstruction but undoubtedly it may contribute to its development.

Chronic idiopathic obstruction of the terminal duodenum with dilatation is a clinical entity and pathologic changes are not necessarily present. Abnormal or variable anatomic factors may aid obstruction in conjunction with a number of functional and neuromuscular disturbances which may be the activating factors. The most necessary factor in the obstruction is probably pressure by the superior mesenteric artery together with the root of the mesentery. Traction on this artery may be produced, clinically, by pelvic displacement of the small intestine.



# TUBERCULOUS PERITONITIS

A STATISTICAL AND CLINICAL STUDY OF ONE HUNDRED AND  
EIGHTY-SEVEN CASES \*

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Although there are numerous monographs and countless shorter articles on the subject of tuberculous peritonitis in the literature, there are relatively few contributions that deal with the disease exclusively as it affects women and in its relation to gynecological conditions. It has been thought worth while, therefore, to give some consideration to this subject, and we have chosen as our means of doing so a statistical study of all patients with proved cases of tuberculous peritonitis treated on the gynecological service of the Johns Hopkins Hospital from its opening on May 7, 1889, until June 30, 1927. In pursuing this study, we have attempted to analyze particularly the types of the disease, both clinical and pathologic, the methods of treatment and the ultimate results. The study of results has not been entirely satisfactory, owing to many difficulties encountered in tracing the subsequent course of patients after their discharge from the hospital. We have, however, obtained data sufficient to admit of some relatively sound conclusions.

## HISTORICAL DATA

It was not until the advent of modern surgical methods had led to frequent laparotomies that anything like an adequate idea of the frequency of tuberculous peritonitis and of its various clinical and pathologic manifestations was reached. The condition had been described in isolated instances as far back as the eighteenth century, Morgagni<sup>1</sup> having published the first satisfactory description of a case in 1744. Two other cases, one by Johnson in 1779, and another by Walther in 1785, were reported in this century, and in the first half of the nineteenth century the pathologic anatomy was described by many of the workers on tuberculosis in general (Bichat, Laennec, Boyle, Louis).<sup>2</sup> During this period, the disease was considered invariably fatal.

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\* From the Gynecological Department, the Johns Hopkins University and Hospital

1 Morgagni: *De sedibus et causis morborum*, epistola 38, no 34, ed Ravius

2 Chavrier Lucien: *These de Paris*, 1895

As early as 1862, Sir Spencer Wells<sup>3</sup> performed a laparotomy on a young woman, aged 22, who was believed to have an ovarian tumor. He found a typical picture of tuberculous peritonitis of the ascitic type, removed the fluid and closed the abdomen. The patient recovered and was well twenty-years after the operation. In 1884, König<sup>4</sup> reported a series of 4 cases in which operation was performed with 3 recoveries, he proposed laparotomy as the method of treatment as soon as the diagnosis should have been made. In 1887, Kummel<sup>5</sup> reported 40 cases with operation and, in 1890, König<sup>6</sup> collected and presented at the Congress of Surgeons in Berlin the cases of 131 patients who had been treated by laparotomy. In this series, there was an apparent cure in 84, or 65 per cent of the cases, but in only 30 of them had a period of two years or more elapsed since the operation.

In this country Van de Warker,<sup>7</sup> in 1887, was the first to advise laparotomy as a method of treatment. He concluded "It is safe to assume that opening the abdomen in instances of tuberculous degeneration of its lining membrane is comparatively free from danger, and, in view of its possible benefit, amply justified."

Thus, surgical intervention gave a tremendous impetus to the study of this disease. In the next few years, many series of cases were reported with the results from operative treatment. In 1892, Lindner reported 205, and Aldibert 308 cases. The following year Roersch collected 358 and Adossides 405 cases. In 1896, Margarucci collected 253 cases of patients operated on by members of the Italian Surgical Society, showing 216 instances, or 85.4 per cent, of cures.<sup>8</sup> Besides the reports of surgical treatment, general consideration of the disease became the subject of numerous studies. Several theses for the degree of Doctor of Medicine at the University of Paris<sup>9</sup> were devoted to the

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3 Wells, Sir Spencer. *Diagnosis and Surgical Treatment of Abdominal Tumors*, London, J & A Churchill, 1885, p. 210.

4 König, F. Ueber diffuse peritoneale Tuberkulose und die durch solche hervorgerufenen Scheingeschwülste im Bauch nebst Bemerkungen zur Prognose und Behandlung dieser Krankheit, *Centralbl f Chir* **11** 81, 1884.

5 Kummel, H. Ueber Laparotomie bei Bauchfelltuberkulose, *Arch i klin Chir* **37** 39, 1888.

6 König, F. Die peritoneale Tuberkulose und ihre Heilung durch den Bauchschnitt, *Centralbl f Chir* **17** 657, 1890.

7 Van de Warker, Elv. Laparotomy as a Cure for Tuberculosis of the Peritoneum, *Am J Obst.* **20** 932, 1887.

8 Johnston, George B., in Kelly and Noble. *Gynecology and Abdominal Surgery*, Philadelphia, W. B. Saunders Company, 1914, vol. 2 p. 617.

9 Alleaume, G. These de Paris 1894. Guillemare, G. These de Paris 1898. Lichteman, S. These de Paris 1896. Clavier (footnote 2).

subject, and in Germany monographs were contributed by Cramer,<sup>10</sup> Lauper<sup>11</sup> and Strassburg<sup>12</sup>

In America in 1890, Osler,<sup>13</sup> published a monograph describing the various clinical and pathologic types of the disease, and, in 1903, Murphy<sup>14</sup> included in a monograph on tuberculosis of the female genitalia a rather complete description of the disease as it occurs in women

Since 1900, the volume of literature has increased rapidly, and it would seem that any merely statistical addition might be superfluous. We find, however, that the subject in its relation to gynecology alone has not been dealt with thoroughly enough to render valueless a few additional statistics. We offer, therefore, the following study of 187 cases as a contribution to the gynecological aspect of tuberculous peritonitis

TABLE 1—*Incidence of Tuberculous Peritonitis*

Time Periods	Patients Treated			Patients with Tuberculous Peritonitis			Percentage Incidence		
	White	Colored	Total	White	Colored	Total	White	Colored	Total
May 7, 1889 to Jan 31, 1890	5,614	935	6,549	30	11	41	0.54	1.18	0.63
Feb 1, 1890 to Jan 31, 1900	6,814	1,990	8,804	33	25	58	0.48	1.26	0.66
Feb 1, 1900 to Jan 31, 1910	6,164	2,989	9,153	22	21	43	0.36	0.70	0.47
Feb 1, 1910 to June 30, 1927	5,009	3,469	8,498	12	33	45	0.24	0.95	0.53
Total—May 7, 1889 June 30, 1927	23,601	9,403	33,004	97	90	187	0.41	0.96	0.56

#### OBSERVATIONS ON ONE HUNDRED AND EIGHTY-SEVEN CASES

*Incidence*—Table 1 is a composite table showing the incidence of tuberculous peritonitis on the gynecological service of the Johns Hopkins Hospital as distributed between the white and colored races and for the different decades since the opening of the hospital in 1889

It will be seen from this table that the incidence for the entire period has been 0.56 per cent. As compared with the general statistics gathered from the literature, this is a remarkably low figure, but it must be taken into consideration that most of the statistics found in the literature are compiled from autopsy rather than from clinical records, and still further that only those women in whom the peritonitis is definitely associated with tuberculosis of the pelvic organs are admitted to the

10 Cramer, C. Ein Fall von Bauchfelktuberkulose, Berlin, G. Schade, 1895

11 Lauper, J. Beitrage zur Frage der Peritonitis tuberkulosa, Leipzig, J. B. Hirschfeld, 1901

12 Strassburg, J. L. A. Ueber Peritonitis tuberkulosa, Kiel, Schmidt & Klaunig, 1902

13 Osler, William. Johns Hopkins Hosp. Rep. 2: 67, 1890

14 Murphy, John B. Tuberculosis of the Female Genitalia, Am. J. Obst. 48: 737, 1902, *ibid* 49: 205, 1902

gynecological service, the others being assigned to either the medical or the general surgical services. In the first 7,000 autopsies at the Johns Hopkins Hospital there were 197 cases of tuberculous peritonitis or an incidence of 2.8 per cent. Engelmann<sup>15</sup> found that in 2,837 autopsies at the Munich Pathological Institute 1.6 per cent and that of 8,421 cases from the Berlin Pathological Institute during ten years 2.5 per cent of the patients had suffered from this disease. In Erlangen during twenty-three years, the autopsy records showed 1.5 per cent and in Kiel 5,425 autopsies in fifteen years gave 1 per cent. These reports include only cases resulting fatally from tuberculous peritonitis. At the Pathological Institute of the University of Prague the statistics of 3,500 autopsies, including the incidental finding of tuberculous peritonitis, gave a percentage incidence of 4.7 per cent.<sup>8</sup> In this country, Cummings,<sup>16</sup> in 3,405 autopsies from the Pennsylvania Philadelphia and University Hospitals, found 92 cases of tuberculous peritonitis (2.7 per cent).

Cummings further found tuberculosis in some form in 835 of the autopsies, or 24.5 per cent, and of these the 92 with peritoneal involvement constituted 11 per cent. In 1,170 autopsies at the Boston City Hospital, Bottomley<sup>17</sup> found tuberculosis in 197 or 16.8 per cent, and tuberculous peritonitis in 14 or 7.1 per cent of these. Nothnagel<sup>18</sup> said that statistics vary from 1.25 to 16.16 per cent of peritoneal involvement among tuberculous patients. He further stated that 24.8 per cent of all cases of peritonitis are tuberculous.

One other point of interest is to be derived from our statistics as presented in table 1, namely, the gradual decline in incidence during the period under consideration. This has been more striking among white than among colored patients. Among the colored patients, the most notable decline was during the third decade with a subsequent slight rise during the past eight years. In the literature we have encountered no similar statistics to compare with our own which, however, are in accord with the figures on tuberculosis in general which has shown a considerable decrease in incidence during the past forty years.

SEX.—Pathologic statistics usually show the disease to be more common in men than in women. Sixty-two of Cummings'<sup>16</sup> 92 cases were in males and 30 in females. In his own series of 21 patients Osler<sup>13</sup>

15 Engelmann F. W. Beiträge zur Kenntnis der Bauchfellentzündung besonders der tuberkulösen Form, Diss. München 1902 p. 34.

16 Cummings, W. T. Univ. Penn. M. Bull. 18 272 1905-1906.

17 Bottomley, John T. Am. Med. 3 265 1902.

18 Nothnagel. System of Medicine quoted by Cummings Univ. Penn. M. Bull. 18 272 1905-1906 quoted by Bottomley Am. Med. 3 265 1902.

found that 15 were males, but he stated that the disease is more common in females, and from the combined figures of Boulland, Hane, Mourange and his own found a total of 60 males and 131 females. In Seik's series of 107 cases, 89 of the patients were males and 18 females. Johnston<sup>8</sup> stated that from the combined statistics of König, Lindner, Kummel and Rosenburg (all surgeons) in 386 cases, only 36 of the patients were men while 350 were women. Thus there is a marked discrepancy between pathologic and operative statistics. As a possible explanation for this Johnston<sup>8</sup> offered that in most pathologic reports no account is taken of the relative number of total autopsies on males and females, and he was of the opinion that the males are usually in larger numbers. We would suggest further that the frequent association in females of peritonitis with tuberculosis of the generative organs and the resulting possibility of successfully extirpating the primary focus at operation lead to operative treatment far more frequently in females than in males, thus accounting for the discrepancy in the statistics on the other side. After reviewing all these statistics, one would be inclined to believe, therefore, that there probably is no very great difference in the incidence of the disease among the two sexes.

*Race*—Oslei<sup>13</sup> stated that it is generally believed that the disease is more common among the colored than the white race but that there are no statistics on the subject justifying any definite decision. Three of his 4 patients at the Johns Hopkins Hospital belonged to the colored race. We also, in reviewing the later literature, have found a striking paucity of figures on this subject. Of 77 cases reported by Cummings,<sup>16</sup> in which the race was stated, 39 were in colored and 38 in white patients, but Cummings gave no figures as to the relative frequency of white and colored in his total of autopsies. Our figures show a decidedly higher incidence among the colored patients. Of our 187 patients, 97 were white and 90 colored, but during the period under consideration there were 23,601 white patients treated on the service and only 9,403 colored patients, so that the incidence among white patients for the total period was 0.41 as compared with 0.96 per cent among colored patients. Greenberg,<sup>19</sup> in a review of 200 cases of tuberculous salpingitis from our service, found an incidence of 0.71 per cent among the white and 1.18 per cent among the colored patients. Thus our figures are in accordance with the general opinion that has been held, but without statistical confirmation as to the greater frequency among the colored race.

*Age*—It is generally stated and confirmed by statistics that tuberculous peritonitis occurs with the greatest frequency between the ages of 20 and 40 years. Table 2 shows our figures on this subject as com-

19 Greenberg J. P. Johns Hopkins Hosp. Rep. **21** 100, 1924

pared with some of the more representative ones collected from the literature

All of the figures in table 2 illustrate clearly that we are dealing with a disease occurring most commonly in young adults. In our own series practically half the patients were between 20 and 30 and 170 of the 187 were between the ages of 10 and 40.

*Parity*—Howard A. Kelly<sup>20</sup> stated that pregnancy has a definite causal relationship to tuberculous peritonitis. In 28 per cent of his cases the onset was definitely dated from a miscarriage or labor. He further stated that of the married women 29.41 per cent remained sterile, and 11.76 per cent miscarried every time, 41.17 per cent were

TABLE 2—*Age Incidence of Tuberculous Peritonitis*

Age Years	Authors Cases		Osler's Cases Collected*		Cummings Cases	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
Under 10	1	0.53	27	8	4	5
10 to 20	47	25.14	75	21.6	14	17.7
20 to 30	92	49.27	87	25.1	17	21.6
30 to 40	31	16.58	71	20.5	17	21.6
40 to 50	10	5.35	61	17.5	12	15
50 to 60	6	3.20	19	5.5	9	11.4
Over 60	0	0.0	6	1.8	6	7.6
Total	187	100	346	100	79	100

\* Osler's cases consist of his own 21 combined with those of Boulland, Hane, Mourange, Fenwick, Bristowe, Hilton, Fagge and Lebert.

TABLE 3—*Number of Pregnancies Among the Ninety-One Parous Women with Tuberculous Peritonitis*

1 in 32	4 in 14	7 in 2	10 in 2
2 in 16	5 in 7	8 in 2	11 in 0
3 in 8	6 in 3	9 in 3	12 in 2

sometimes delivered at term and sometimes had miscarriages, while but 17.64 per cent always went to term.

In our series, there were 51 unmarried women and 136 who were or had been married, 87 were nulliparous, 91 had borne one or more children, and in the histories of 9 there was no statement in this regard. The number of pregnancies among the 91 women who had borne children is shown in table 3.

Only 10 of the women are recorded as having had abortions. In 27 cases or 14.5 per cent, the onset occurred during or followed within a short time after the termination of a pregnancy, while in a parous woman who had had 7 pregnancies the tuberculous peritonitis did not come on.

<sup>20</sup> Kelly, Howard A. *Operative Gynecology*. New York: D. Appleton & Company, 1906, vol. 2, p. 237.

until nineteen years after the termination of the last one. Of the 27 in whom the onset was associated with pregnancy, in 6 the pregnancy ended in a miscarriage.

*Contact*—The history of contact with tuberculous persons is absent in a strikingly large percentage of our patients. Only 38 gave a definite family history of tuberculosis, while 131 absolutely denied any ascertainable source of contact. In 18 histories there was no record regarding this point. In Kelly's<sup>20</sup> 16 cases there was a tuberculous family history in only 2. Bottomley<sup>17</sup> found a definite family history in only 2 of 25 cases. These figures are rather confirmatory of the accuracy of our own, about which, however, we are still inclined to some skepticism on account of the gross ignorance of many of the patients included in our series.

*Symptomatology*—The disease presents great variations in its clinical manifestations, and in the degree of its severity. There are several definitely distinct pathologic varieties which we shall discuss

TABLE 4—*Duration of Symptoms*

Less than 1 month	17	7 months	3	3 to 4 years	6
1 month	12	8 months	11	4 to 5 years	11
2 months	12	9 months	9	5 to 6 years	2
3 months	11	10 months	1	6 to 7 years	2
4 months	15	11 months	4	8 years	1
5 months	6	1 to 2 years	27	10 years	1
6 months	13	2 to 3 years	16	Questionable	6

later, and the symptoms and clinical course vary considerably with these forms. From a purely clinical point of view, regardless of pathologic changes, certain definite observations may be made.

In the first place, the onset may be sudden with severe symptoms of an acute illness which may terminate fatally or pass over into a chronic form. On the other hand, the onset may be insidious and symptoms may progress slowly so that months or even several years may elapse before the patient finally seeks medical assistance. In our series of cases, 73 patients had noticed their symptoms for a year or more when they first came to the clinic, while 114 suffered severely enough to induce them to seek aid within the first year. In 17 of these the symptoms were so acute as to bring them to the clinic within the first month after onset. Table 4 shows the duration of symptoms in the 187 patients at the time they first presented themselves at the clinic.

Osler<sup>13</sup> stressed the point that the symptoms may be quite latent and cited several cases in which the condition was discovered during the course of autopsies on patients who had died of an entirely different malady and in whose cases there had been no suggestion of a tuberculous peritonitis during life. On the other hand, he also stressed a

group of cases in which the onset is so sudden that the disease is apt to be confused with some condition more commonly acute, such as enteritis, hernia or simple acute peritonitis. In analyzing our cases according to the severity of symptoms and signs it was found that 25 could be considered as acute, 31 subacute, 119 chronic, 7 as chronic with acute exacerbation at the time of admission and 5 as latent. These figures, together with those in table 4, seem to indicate clearly that in the majority of cases the disease runs a chronic course, while in a small minority the symptoms are those of an acute illness.

Later in this paper we shall classify our cases pathologically according to Murphy's<sup>14</sup> groups I, III and IV, omitting his group II. The three groups that we have found it convenient to use are I, the disseminated, exudative, miliary, nonconfluent serous (ascitic) variety, III, the adhesive, fibroplastic, cystic, partition or obliterative variety, and IV, tuberculous peritonitis with mixed or secondary infection. In group I there are 42, in group III, 108 and in group IV, 12 cases. The remaining 25 cases could not be classified because of insufficient data due to the fact that in the majority no operation was performed. We have thought it worth while at this point to attempt a correlation between these pathologic groups and the several clinical varieties such as acute, chronic and latent. Accordingly, of the 42 cases in group I 6 were acute, 7 subacute, 28 chronic and in 1 the process was entirely latent, giving rise to no symptoms whatever. Of the 108 cases in group III, 6 were acute, 14 subacute, 82 chronic and 3 chronic with an acute exacerbation. In group IV, those with secondary infection, all the patients were acutely ill. Thus it is seen that, with the exception of group IV, the great majority of cases are chronic regardless of the pathologic type, but that the percentage of acute cases in group I (14.3) is somewhat higher than that in group III (5.5). This is of some significance as it will be seen later that a case which in the early stages presents a picture characteristic of group I will later present the features of the more frequently chronic group III.

*Chief Complaint*—In analyzing the chief complaint with which the patients presented themselves, it is found that in the vast majority of the cases pain in one form or another was the determining factor that brought the patient to the clinic. In fact 161 of the 187 patients complained of some form of pain, usually located in the abdomen. A variety of other symptoms were also sufficiently annoying to be mentioned with the chief complaint. These were sometimes complained of alone but more often in association with pain. Table 5 gives the varieties as to character and location of the pain complained of and in table 6 will be seen the various other more or less prominent symptoms.

There is little of diagnostic value to be learned from the facts presented in table 5. The types of pain complained of are such as



commonly accompany a variety of intra-abdominal conditions. Table 6, however, is somewhat more helpful, in that it shows abdominal swelling to be a symptom rather frequently observed by the patient. Abdominal swelling, particularly when it can be proved to be due to ascites, is strongly suggestive of one of several conditions: tuberculous peritonitis, cirrhosis of the liver, carcinomatosis, flaccid ovarian cyst, fibroma of the ovary associated with marked ascites or general anasarca due to cardiac or renal disease. All of these conditions except the first are apt to occur in persons of at least middle age. Our statistics, however, show tuberculous peritonitis to be far more common in younger per-

TABLE 5—*Varieties of Pain Mentioned in Chief Complaint*

Abdominal pain	54	Headache	5
Lower abdominal pain	41	Drawing abdominal pain	2
Right lower quadrant pain	13	Pain around umbilicus	2
Back ache	13	Shooting lower abdominal pain	1
Abdominal soreness	10	Pain in right hip	1
Left lower quadrant pain	5	Pain in left flank	1
Abdominal cramplike pain	5	Chest pain	1
Dysmenorrhea	5	Pain of various types, total	161

TABLE 6—*Other Symptoms Mentioned in Chief Complaint*

Abdominal swelling	53	Diarrhea	2
Weakness or susceptibility to fatigue	13	Loss of weight	2
Nausea and vomiting	7	Frequency of urination	2
Dysuria	6	Fecal fistula	2
Abdominal mass	6	Postoperative fistula	2
Amenorrhea	5	Hemorrhoids	1
Menorrhagia	5	Malaise	1
Fever	5	Nosebleed	1
Dragging sensation	4	Draining umbilical sinus	1
Leukorrhea	3	Postoperative ventral hernia	1
Prolapsus	3	Indigestion	1
Constipation	3	Convulsions	1
General ill health	2	Urinary retention	1

sons. Certainly in a young person with evidence of ascites, tuberculous peritonitis should be considered as a strong possibility.

Weakness or susceptibility to fatigue, when persisting over a long period of time, should always arouse one's suspicions of a tuberculous condition, but this symptom was mentioned by only 13 patients among their chief complaints. The various types of fistulas or draining sinuses mentioned by 5 patients are symptoms which should also entail a careful search for a tuberculous process. The others listed in table 6 are either of no significance or will be considered later along with the general symptomatology.

Many symptoms not particularly stressed in the chief complaint were found on further questioning to be of more or less frequent occurrence. We have attempted to tabulate the symptoms as obtained

from the histories under four headings (1) general symptoms, particularly those such as one should expect to find associated with a tuberculous condition, (2) digestive symptoms, (3) gynecological symptoms, and (4) urinary symptoms. Table 7 gives the relative frequency of various symptoms occurring under these headings.

From this table we again see the striking preponderance of pain as a symptom but draw no further diagnostic aid from it except as it can be linked up with more specific symptoms.

Fever and loss of weight are suggestive of a tuberculous condition, particularly if the fever is moderate and the temperature shows an afternoon rise. As has already been said the presence of ascites in a young person is always suggestive of tuberculous peritonitis and if this is associated with fever and loss of weight the evidence becomes increasingly strong. A history of chronic cough or hemoptysis is important as a possible indication of pulmonary involvement. A history of pleurisy was obtained in 20 and there was definite pulmonary involvement in 40 of our cases.

TABLE 7—*Symptomatology of Tuberculous Peritonitis*

1 General		2 Digestive		3 Gynecologic		4 Urinary	
Pain	162	Nausea and vomiting	51	Irregular or increased uterine bleeding	40	Dysuria	91
Fever	142	Nausea without vomiting	10	Amenorrhea complete	40	Frequency	41
Loss of weight	115	Constipation	78	Scanty flow	26	Hematuria	6
Ascites	83	Diarrhea	13	Leukorrhea	122		
Cough	48	Constipation and diarrhea alternating	2	Dysmenorrhea	54		
Hemoptysis	11						

The digestive symptoms, again, are far from specific, and are such as may be found with a variety of intra-abdominal conditions. Kelly<sup>20</sup> stressed constipation as occurring in one half of his patients and stated that 20 per cent complained of pain on defecation. These symptoms are easily explainable on the basis of large pelvic masses exerting pressure on the rectum. Seventy-eight patients in our series were troubled with constipation. Diarrhea occurring alone as in 13 or alternating with constipation, as in 2 of our cases is more apt to occur when there is actual disease of the intestinal tract. Nausea and vomiting occur more frequently in those cases in which there is a widespread dissemination of the peritoneal process with extensive involvement of the upper part of the abdomen. In considering the digestive symptoms it must not be lost sight of that other diseases of the gastro-intestinal tract such as ulcer, disease of the gallbladder or appendicitis may be present simultaneously with the tuberculous peritonitis and although as has been shown varied and marked digestive symptoms may be produced by this disease alone one should never fall into the error of assuming without proof that all of a patient's symptoms are due to a single morbid entity.

Menstrual disturbances of one kind or another aside from dysmenorrhea were noted in 106 cases. Forty of these patients had irregular or excessive uterine bleeding, which is of no great diagnostic aid since it is a symptom of so many different pelvic disorders. However, a complete amenorrhea in 40 patients and a scanty flow in 26 are more worthy of note. These should always lead one to look for tuberculosis, particularly tuberculosis of the genital organs, since they are symptoms which will result from a destructive process in either the ovaries or the endometrium, but on the other hand may also result from any wasting, debilitating, systemic disease. Leukorrhea occurred in 122 patients, but again this is a symptom common to many conditions. On the other hand, a profuse leukorrhea when associated with amenorrhea is suggestive.

Kelly<sup>20</sup> stated that pain on urination is the most characteristic of all the symptoms and found only 3 of 20 patients free from it. In our series not quite half the patients were troubled by this symptom, while only 41 complained of frequency. We have found no adequate explanation for the frequency of these symptoms, but it seems logical to assume that, in the adhesive variety of peritonitis adhesions between the bladder and other viscera might easily account for either one or both of them, while in the ascitic variety the pressure of abdominal fluid on the bladder would naturally lead to frequency. The presence of hematuria, which occurred in 6 of our cases, should always arouse a suspicion of renal tuberculosis, and in 2 of the 6 this lesion was actually demonstrated.

Owing to the diversity in the manifestations of the disease, clinical as well as pathologic, it is difficult to regard any single symptomatic syndrome as definitely characteristic. From our own experience, however, we believe that the presence of abdominal swelling and distention, particularly if there is definite ascites and a history of pleurisy, associated with abdominal pain or pelvic pain which is worse at the menstrual periods, with a low grade fever, higher toward evening, and loss of weight, with some digestive symptoms especially constipation, and with dysuria or frequency, or both, constitute a syndrome which should strongly arouse the clinician's suspicion of peritoneal tuberculosis. If in addition to these symptoms there is a menstrual disturbance, more particularly an amenorrhea or scanty flow combined with a profuse leukorrhea, the evidence becomes very strong.

Murphy<sup>14</sup> stressed the fact that in the serous ascitic variety of the disease alternate remissions and exacerbations of symptoms are frequently observed. He attributed the exacerbations to intermittent showers of tubercle bacilli thrown into the peritoneal cavity along with caseous material extruded from the patent fimbriated ends of the tubes.

This is a phenomenon well worth noting in observing the clinical course of these patients, and it has already been stated that 7 of our patients who gave a history suggestive of a chronic course were admitted during such an acute exacerbation

*Signs*—In addition to the subjective symptoms complained of by the patient the observations on physical examination particularly those referable to the abdomen and pelvis, were noted. On abdominal examination, tenderness was noted in 101, distention in 83 signs of free fluid in 53 and palpable masses in 42 patients. Pelvic examination revealed a variety of observations with various combinations. Table 8 gives a list of the various signs noted with their frequency.

It will be readily seen from the list in table 8 that there is nothing specifically to be made out from pelvic examination which can be considered characteristic of the disease. In rare cases tubercles were

TABLE 8—*Observations from Pelvic Examination*

Bilateral indurated masses	59	Thickened vaginal wall	5
Pelvic adhesions and immobility	37	Tubercles or nodules felt per rectum	5
Pelvic tenderness	29	Tubercles palpable per vaginam	4
Unilateral indurated masses	25	Mycomas	3
General pelvic induration	24	Thickened ureter*	1
Bulging masses in culdesac	19	Vaginal fecal fistula	1
Malposition of uterus	13	Tubercle like nodules in cervix	1
Cystic masses	12	Rectal stricture	1
Relaxed vaginal outlet	12	Pelvic examination entirely negative	19
Indurated or thickened tubes	8		

\* Years ago Leslie M. Sweetnam drew attention to the fact that a thickened ureter felt per vaginam almost invariably indicates a tuberculous kidney. (Personal communication from Dr. Thomas S. Cullen.)

actually palpated by rectum or by the vagina but the percentage of cases in which this observation was noted is so small as to be of little significance. The other observations were all such as might belong to a great variety of pelvic conditions.

*Pulmonary Tuberculosis*—On admission to the hospital 59 patients were suffering from a more or less active pulmonary tuberculosis or had a history of a recent pleurisy. Postoperative pleurisy was a complication of convalescence in 9 patients. An operation was performed on all patients in whom pulmonary activity was not sufficiently marked to make a short anesthesia unjustifiable. The final results in the cases that we have been able to follow up are tabulated later, with a note as to the presence or absence of active pulmonary disease.

The longer one works over the records of this group of patients with peritoneal and pelvic tuberculosis, the more does it seem likely that most of these patients may fairly definitely be considered as having had an original pulmonary focus from which all their trouble began regardless of whether or not it was demonstrated during their stay in

the hospital. This is just an impression one gains from observing the frequency with which an anesthetic stirs up an acute pleurisy, and the greater frequency with which active or old pulmonary disease is demonstrated in the more recent cases, especially since the use of the roentgen ray as a diagnostic adjunct.

*Tuberculosis Elsewhere*—Aside from the lungs, pleurae and peritoneal cavity, tuberculosis was found elsewhere in only a few cases. A definite tuberculous cervical adenitis was demonstrated in only 4 cases, though in a good many others there was a positive statement as to the enlargement of cervical glands, the nature of this enlargement, however, being uncertain. There was involvement of the kidneys in 2 cases, as shown at autopsy, after being diagnosed clinically by the presence of bacilli in the urine. In one of these a psoas abscess with involvement of the lumbar vertebrae was also found. In one case the autopsy showed a tuberculous otitis media and disseminated tubercles in the liver and spleen. Three patients died of either miliary tuberculosis or meningitis. Autopsies were obtained on all of these. One had a generalized miliary disease with meningeal involvement, another meningitis without the wide dissemination and the third a combination of the two. All of these patients except the 4 with adenitis, belong in the acute, desperately ill group.

*Diagnosis*—The correct preoperative diagnosis was made and recorded in the history in 50 cases, or 27 per cent. In 115 instances the preoperative diagnosis was not specifically mentioned, but there can be little doubt from the description that the condition was recognized in many of these. In this group also are the cases in which tuberculosis was not recognized, but an operation was performed for myomata uteri, repair of a hernia, appendicitis, malpositions of the uterus, ovarian cysts and other conditions. A large percentage was apparently operated on for supposedly tuberculous salpingitis, when diseased tubes had been felt on pelvic examination, but there had been no clinical manifestations of the peritoneal dissemination. It is common for these patients to be in good physical condition, and this led to confusion in a few instances. In 14 patients the preoperative diagnosis was specifically stated as chronic salpingitis and the tuberculous nature was first discovered at operation.

The correct diagnosis in the 50 cases was made most frequently in the patients with ascites and abdominal tenderness and in whom a history of a recent pleurisy was obtainable, or pulmonary tuberculosis was demonstrable. In some of the cases with a history of bleeding tuberculosis was discovered in the endometrium removed by curettage, and a laparotomy was later performed. In 2 instances tubercles were felt

on the peritoneal surfaces of the pelvis on rectal examination, and in 1 instance through a posterior colpotomy wound. In less advanced tubal cases the diagnosis was suggested occasionally from discrete nodules palpated along the course of the tubes. In advanced tubal cases the peculiar matted feeling of the pelvic viscera sometimes suggested tuberculosis.

The interpretation of the various abdominal tumors occurring in this series shows that in only 1 instance was there an elongated mass in the epigastrium interpreted as rolled up tuberculous omentum detected before operation—a condition so frequently mentioned in the literature. Localized accumulations of fluid were mistaken for ovarian cysts in 4 cases, and to explain the fixation in 1 case it was thought probable that the cyst was parovarian. One patient with much tenderness over the mass was thought to have a cyst with a twisted pedicle. Carcinoma of the ovary with abdominal metastases was the preoperative diagnosis in 3 of the patients past middle age.

*Focus of Peritoneal Infection, Tuberculous Salpingitis*—In all but 9 of the 94 cases in which one or both tubes were removed tuberculosis was reported specifically in these structures. The clinical and gross pathologic diagnosis was certain in these 9, but a superimposed acute infection made the histologic diagnosis uncertain. Therefore, in 85 cases, or 45 per cent of the total series, tuberculosis of the tubes was proved to be present, and probably was the original focus in the peritoneal cavity. There were many interesting variations in this group. An occasional abdomen presented more active and more marked tuberculosis in the upper portion with small closed off tubes, which on section showed a chronic process, suggesting that the pelvic process was healed or in process of healing while activity was still continuing in the upper part of the abdomen. In one of these a diverticulum of the large bowel was present in an area much affected and suspicion was directed to this as a focus. On section however the tubes showed a chronic tuberculous process. Similar cases were those with the appendix much involved but also with tuberculous tubes.

In at least 3 cases large tuberculous peritoneal cysts were described with the open fimbriated extremities of one or both tubes opening into them.

There are two groups of cases in which it seems impossible to tell whether the tubes are the original pelvic focus or not. One group includes those patients with an advanced and severe peritoneal process in whom the tubes could not be seen during operation and in whom all pelvic structures were diseased. The other is the disseminated ascitic type of case in which the patients have a uniform distribution of

tubercles over the abdomen, or perhaps a more prominent distribution in the upper part of abdomen, and in whom the tubes were not removed. As will be seen, there were a few, 6 to be exact, of the latter group in which an exploratory laparotomy was first done and symptomatic tubal disease developed later, requiring a second operation. It is certain, however, that this does not always happen.

*Tuberculosis of the Endometrium*—In 66 instances the endometrium was available for examination, either because a diagnostic curettage was done for bleeding or because the uterus was removed. Thirty-seven of these showed a tuberculous involvement of the tissue. The association with symptomatic uterine disorders in the 37 cases was as follows: leukorrhea, 24, amenorrhea, 20, metrorrhagia, 2, menorrhagia, 7, while in 8 of the patients the periods had been normal.

It is thus seen that leukorrhea is most commonly associated with tuberculosis of the endometrium. Amenorrhea also occurs frequently but it would seem unwise to attribute its presence to the endometrial disease alone, for 5 of these patients had advanced pulmonary tuberculosis, and several had marked involvement of both ovaries with probable destruction of their function. Infantilism of the genital organs, which is often stated in the literature as frequently associated with tuberculosis of these organs, was noted only once in this series.

In the entire series, 22 of 68 patients with clinically active pulmonary, bone or urinary tuberculosis had had amenorrhea. As a rule, this symptom accompanied the more advanced cases, and was often met with in patients who could not be operated on because of the extent of the pulmonary process. We have proof in only 5 of these that the endometrium was tuberculous.

*Pathologic Types*—In 1903, Murphy<sup>14</sup> divided the lesions of tuberculous peritonitis into four groups on a pathologic basis as follows:

I The Disseminated, Exudative, Miliary, Nonconfluent Serous (Ascitic) Variety. The tubes in this group are usually patent and caseous material may be expressed from their lumina. The pelvic peritoneum bears the brunt of the infection, but the whole peritoneal cavity may be involved. Ascitic fluid, clear yellow, slightly sanguineous, or a little cloudy, from a few ounces to large quantities, may be present.

II The Nodular Ulcerative or Perforative Variety, the Least Common Type. In this variety, the whole force of the destructive process is concentrated into small areas, and in these areas not only the peritoneal coat but the deeper structures, as the intestinal wall, the mesentery, uterus or ovaries, are destroyed or changed into caseous masses surrounded by dense connective tissue barriers or adhesions. The tubes are usually closed or fixed at their fimbriated ends to the adjacent viscera.

III The Adhesive, Fibroplastic, Cystic, Partition or Obliterative Variety In many cases this group represents the healing stages of the disseminated ascitic variety, but it has been pointed out that these adhesive varieties sometimes arise without previous ascites. In this group occur the bizarre tumors of localized accumulations of fluid, rolled up omentum, etc. The tubes are closed with adnexal masses often present. Fresh adhesions are fibrinous in character, the older cases present very tough fibrous bands uniting contiguous structures.

IV Tuberculous Peritonitis with Mixed Infection A secondary infection may be superadded to cases belonging to any of the preceding types. The colon bacillus is a common invader, and a localized or a fairly general peritoneal infection may occur. This group of patients presents the most severe and even desperate form of the disease, death frequently occurring as an immediate result of the secondary infection. If surgical drainage is instituted promptly some may live, but fistulas frequently follow the necessary use of drains.

Three of the groups described by Murphy (groups I, III and IV) are common and seem to us useful in helping to visualize the processes that take place within the abdomen, and in understanding the various manifestations of the disease. We have found classification of our cases according to this scheme practical in a large proportion of them but when for want of adequate description in the hospital record or because the abdomen was not opened or could not be thoroughly explored, the group is in doubt, we have omitted such cases (25 in our series) from the classification.

We have tabulated 42 cases as fairly clearly belonging to Murphy's group I, but it must be made plain that, although in the hospital histories explicit notes were not made in all cases as to the patency of the tubes no large masses were found in the pelvis. Classification was possible in such cases on the basis of general dissemination of tubercles and the presence of ascites. We have frequently an overlapping of the simple ascitic cases (group I) with those of group III in which pelvic masses have formed and the abdomen is being obliterated or partitioned off by adhesions. In fully half a dozen cases this change was nicely exemplified at operations a few months or a year or so apart, a case which had appeared as belonging to the simple ascitic variety at the first operation presenting the features of an adhesive or cystic partition variety at the second.

None of the patients with the simple ascitic variety died in the hospital. There did not seem to be a tendency for the fluid to reaccumulate to an extent sufficient to make further surgical procedures imperative. Of the 42 patients 5 died of pulmonary tuberculosis within five years after leaving the hospital. Twenty are living and well and



the remaining 17 could not be traced. The operation most frequently performed in this group was a simple exploratory laparotomy with evacuation of the ascites and removal of a bit of tissue for pathologic confirmation of the clinical diagnosis.

We have put none of our cases in Murphy's group II, because we could never feel sure that any of them coincided with his idea of the nodular ulcerative variety. However, we think that if some of the severe generally disseminated cases that we have placed in groups III and IV could have been seen at an earlier stage, they probably would have fallen into this group.

To group III, the fibroplastic variety, we have assigned 108 cases. The most frequent type in this group was found to be that in which there were adnexal masses and a dissemination of tubercles. In a few there was generalized ascites and in many there were localized accumulations of fluid. The most characteristic observation was wide-spread

TABLE 9—*Treatment of 187 Patients with Tuberculous Peritonitis*

Operation	Number	Previous Operations	Died in Hospital	Subsequent Operations	Living After Discharge	Died After Discharge	Untraced
No operation	17	0	5	0	2	2	8
Posterior colpotomy	12	1	5	11	3	0	4
For fistulas	6	6	2	0	3	0	1
Exploratory laparotomy	74	6	11	6	15	3	14
Operations conservative	28	5	1	3	8	4	15
Complete pelvic operation	66	7	5	3	20	8	33

abdominal adhesions. In general these were cases of longer standing than those in group I, and the clinical course was more apt to be of a chronic, sometimes even of a latent, nature. The operation most frequently performed was removal of the diseased pelvic structures when possible, otherwise an exploratory laparotomy with evacuation of the cystic accumulations of the fluid was carried out.

Six of the patients belonging to this group died in the hospital, 1 of shock, 2 of intestinal obstruction, 1 of acute secondary peritonitis, 1 of generalized tuberculosis and 1 of pulmonary embolus. We have been able to trace 21 patients from this group who are still living. In most of these the pelvic focus was entirely removed, but 1 is living after thirty-five years in whom the pelvic masses were so extensive that it seemed unwise to attempt to remove them.

We have 12 cases in the secondarily infected group (IV). The patients were all desperately ill and operation was undertaken only as a last resort. They all died in the hospital either as an immediate result of the preexisting infection or from fistula formation and inanition following surgical drainage.

It must again be repeated that because of overlapping of disease types, confusion in the records and other reasons these figures are all only approximations

*Treatment*—The treatment of 187 patients with tuberculous peritonitis is given in table 9. All but 17 of these women were operated on. For 170 patients, we have 185 operations. The table represents operations, not patients.

*No Operation*—Seventeen patients were not operated on. The diagnosis of tuberculous peritonitis in these, however, seems clear because of the combination of unmistakable signs of pulmonary and abdominal tuberculosis. All but 2 had advanced pulmonary tuberculosis or acute pleurisy and were transferred to the medical service of the hospital or to sanatoriums for treatment. The remaining 2 had advanced renal tuberculosis at the time of their admission or previously. Five died in the hospital, 3 of advanced pulmonary and generalized tuberculosis, 1 of hemorrhage from the intestinal tract and 1 of advanced renal tuberculosis.

Twelve left the hospital. Only 2 are known to be living today. One (eight years after discharge) is in good health so far as we can ascertain. Another is living after three years, practically all spent in a sanatorium, but is not well, although the abdominal symptoms have disappeared, and there are no masses palpable on pelvic examination. We know that 2 died from advanced pulmonary tuberculosis within a year after leaving the hospital. Eight could not be traced.

*Posterior Colpotomy*—This operation was performed one or more times on 12 patients for accumulations of fluid or pus in the culdesac. All of these patients except 1 were submitted to an abdominal operation. Section had been performed six months and nine years previously in 2 cases, was performed at the time of the posterior colpotomy in another, the remainder following posterior colpotomy from one month to a year. In the patient who did not come to abdominal section the diagnosis was made from the shothlike tubercles palpable over the peritoneal surfaces in the pelvis at the time of the posterior vaginal puncture.

Five died in the hospital following abdominal section. Four died of fistula formation and irritation. One died of a colon peritonitis. Simple exploratory laparotomy and drainage were done in 4 of those who died. In the other both tubes were removed.

Seven left the hospital. Of these 4 had undergone a complete operation. In 2 an exploratory laparotomy had been performed. In 1 case no secondary operation was done. Three are living and well after complete operations. Four cannot be traced.

**Closure of Fistulas** Four patients with tuberculous peritonitis were operated on for chronic fecal or urinary fistulas, having previously had 1 or more operations elsewhere. Two were cured, 1 was improved and 1 died after a resection of a portion of the terminal ileum.

After abdominal drainage for secondary infection, two patients developed fistulas. In closing one of these it was necessary to resect the cecum. Both patients died.

**Exploratory Laparotomy** Simple exploratory laparotomy with excision of tissue was performed 73 times for one or more of the following reasons: (1) for drainage in desperately ill, secondarily infected patients, or to evacuate an ascites, (2) when removal of large pelvic masses seemed hazardous, (3) when the tubes looked patent and it was wished to preserve the child-bearing function if possible, (4) by choice—to prove the therapeutic result of simply opening the abdomen.

Six of these patients had undergone a posterior colpotomy one or more times before the abdomen was opened. The punctures were done for pelvic accumulations of pus in 4 cases, in all of which the outcome was eventually fatal. Two were done for accumulations of clear fluid in the culdesac.

Drainage was employed in 25 cases. Eight of the patients were desperately ill from secondary infections. In 17 there was no obvious secondary infection. In the 25 are included the earlier cases of the hospital when drainage was employed as a routine measure. Sufficient commentary on the question of drainage is supplied by the fact that at the present time drains are never employed in tuberculous cases except when necessary for secondary infection or to control bleeding. When drains are used, the immediate postoperative course is apt to be more difficult, incisions break down oftener with danger of hernia or fistulas develop. Thirteen of the 25 cases, in which drains were used, were complicated. In 6, draining sinuses persisted for a long time. The remaining 12 seem to have been uncomplicated as far as can be gathered from the hospital records.

Eleven of these 73 patients died in the hospital. Eight were desperately ill when admitted, suffering from the secondarily infected variety of the disease, and died of infection or of fistula formation and manition. One died of shock, 1 of intestinal obstruction and another of peritonitis following accidental perforation of the adherent small bowel during the posterior colpotomy.

The remaining 62 left the hospital well or improved. Seven are known to have undergone subsequent operations. Five did not get well until the tubes were removed. One of these had no trouble for eight

years, but finally underwent a salpingectomy nine years after the exploratory laparotomy. In 4 of the 5 the tubes looked normal at the time of the original operation, but were considerably involved at the time of removal. One patient was submitted to a complete operation two years after the exploratory laparotomy. In 1 case two pelvic punctures were performed within six months after the exploratory laparotomy.

Four of the patients who left the hospital are dead. Two died of pulmonary tuberculosis within two years. One died of intestinal obstruction twenty-seven years after operation. The cause of death in the fourth, nineteen years after operation, is unknown.

Fifteen are living and well from eighteen months to thirty-five years after operation. In only 3 of these was gross tubal involvement found at the time of operation. In the others the disease was of the discrete disseminated variety with patent tubes and ascites. None have become pregnant.

Forty-three could not be traced.

**Conservative Surgical Intervention.** Twenty-eight patients were submitted to various forms of conservative pelvic surgical intervention. Both tubes were removed in all except 6 cases in which one tube was left or plastic work was performed. The tubes were removed following exploratory laparotomy in 4 cases. They had appeared normal at the original operation and were not thought to be the focus of the tuberculous infection. Drainage was employed in 5. Two of these are recorded as acquiring persistent sinuses. The other 3 in 2 of which pelvic drains were used, suffered from no complications.

One of the 28 died in the hospital, a patient with a severe secondary infection on whom a laparotomy was performed following posterior colpotomy. Twenty-seven left the hospital. Three were operated on again later. Two underwent complete operations because of continued severe pain. The third had painful adhesions which were released. A fourth six months after plastic work on the tubes had been advised to have another operation because of persistent symptoms.

Four of the 27 are dead. One died of pulmonary tuberculosis within a year. Another died of pulmonary embolus following cholecystectomy four years after salpingectomy. The cause of death in the other 2 is unknown—nine and two years after operation. Seven are living and well from 1 to 30 years after operation. Fifteen cannot be traced.

**Complete Operation.** Both tubes and ovaries were removed in 66 cases. These represent as a rule the severer forms of the disease for ovaries were saved whenever possible. In all but a few of these patients the uterus was also removed. Panhysterectomy was performed 10 times; supravaginal hysterectomy 51 times.

Four operations with removal of all the internal generative organs followed one or more posterior colpotomies. So far as we can ascertain, the complete operation was done after previous conservative surgical intervention in only 2 cases—both for continued severe dysmenorrhea—and in only 1 case following an exploratory laparotomy.

Drainage was employed in 34 of these operations. Pelvic drains were employed in 25 cases and abdominal drains alone or combined with the pelvic drains in 12 cases. Wound infection, sinuses or fistulas occurred in 8 cases. A high postoperative fever was also noted in some. In the 32 cases in which drainage was not performed, wound infection, sinuses or fistulas are recorded only four times. Of course, it was only in the worse cases that drainage was instituted, in some after accidental injury to the rectum. Five of these patients died in the hospital, the causes being generalized tuberculosis 2, pulmonary embolus, 1, secondary peritonitis in a diabetic patient 1 and intestinal obstruction, 1.

Sixty-one left the hospital well or improved. In 2 a second laparotomy was done later for release of adhesions. In 1 case a posterior colpotomy was performed later for an accumulation of fluid in the pelvis.

We know that 8 died from 1 month to five years after operation, and in 4 cases we have definite knowledge that the death was due to pulmonary tuberculosis. Twenty are alive and well from a few months to thirty-four years after operation. Thirty-three cannot be traced.

## RESULTS

Before beginning a tabulation of the results, a brief comment may be made on the difficulties that we have encountered in tracing the subsequent course of the patients after their discharge from the hospital. It will be seen by reference to table 9 that 104 of the 187 patients are untraced, but when we consider that our statistics extend over a period of thirty-eight years and that 90 of our patients were negroes and many of the whites were from among the foreign element, the difficulties in tracing them become obvious. This part of the work has been diligently pursued over a period of more than two years, and every available means has been employed to trace the patients, so that the failure to find 104 of them is rather disappointing. Letters were first sent to every possible address obtained from the ward and dispensary records of the patients. After these letters had been returned, an attempt was made personally to seek out the patients who had given Baltimore addresses. This method was effective in collecting data on a few additional cases but in many it was found that the district had been absorbed by industrial expansion. In other cases addresses were

TABLE 10—Type of Disease and Operation and Cause of Death in Twenty-Six Patients

Number	Pulmonary Activity	Days in Hospital	Type of Peritoneal Disease	Operation	Cause of Death
U 12337	No	10	Disseminated secondary infection	Exploratory laparotomy closure of tuberculous perforation	Secondary infection
U 9911	No	65	Disseminated secondary infection	Exploratory laparotomy closure of fistula	Fecal fistula and inanition
U-5712	No	55	Disseminated secondary infection	Posterior colpotomy exploratory laparotomy	Fecal fistula and inanition
36544	No	63	Disseminated secondary infection	Posterior colpotomy exploratory laparotomy	Fecal fistula and inanition
27976	No	47	Adhesive	Complete pelvic operation	Diabetes localized infection
27504	Yes	32	Localized secondary infection	Drainage of abscess resection of cecum	Fecal fistula generalized tuberculosis
26955	Yes	40	Disseminated secondary infection	Posterior colpotomy conservative pelvic	Infection and military tuberculosis
25345	No	1	Chronic adhesive	Exploratory laparotomy	Shock
24669	No	6	Disseminated pelvic masses	Complete pelvic	Pulmonary embolus
22954	No	23	Chronic adhesive	Complete pelvic	Generalized tuberculosis
21769	Yes	2	Disseminated pelvic abscess	Exploratory laparotomy	Secondary infection
18887	No	43	Disseminated secondary infection	Posterior colpotomy exploratory laparotomy	Fecal fistula and inanition
17589	Yes	19	Chronic adhesive	Complete pelvic enterostomy	Intestinal obstruction
17261	Yes	14	Disseminated pelvic masses	Complete pelvic	Pulmonary tuberculosis
15499	Yes	1	Generalized	None	Generalized tuberculosis
14667	?	7	Disseminated secondary infection	Exploratory laparotomy	Secondary infection
13623	No	69	Disseminated pelvic abscess	Exploratory laparotomy curettage of fistula	Fecal fistula and inanition
12908	No	4	Disseminated secondary infection	Exploratory laparotomy colostomy	Secondary infection general tuberculosis
10895	Yes	6	Disseminated	None	Generalized military tuberculosis
9966	No	97	Disseminated secondary infection	Left nephrectomy	Uremia generalized tuberculosis
6884	No	5	Adhesive secondary infection	Complete pelvic	Secondary infection
6299	Yes	16	Intestinal ulcers generalized	None	Intestinal hemorrhage
5240	No	18	Generalized pelvic abscess	Posterior colpotomy exploratory laparotomy	Secondary infection
41651	?	2	Disseminated secondary	None	Pneumonia general tuberculosis
1388	?	70	Chronic adhesive	Complete pelvic resection of adhesions	Intestinal obstruction
500	Yes	7	Disseminated	None	Generalized tuberculosis

found to be those of boarding houses at which out-of-town patients were staying when admitted to the hospital. This method is often adopted by certain colored patients from other states in an attempt to secure free admission. We feel, therefore, that though the results obtained are disappointing, the facts that we have been able to collect are probably from the more intelligent of the series and therefore probably of as much value as from a larger group.

*Died in the Hospital*—Twenty-six patients died in the hospital. Five of these were not operated on. The operative mortality rate is then 11.3 per cent. The major causes of death in the patients operated on are as follows: (1) fecal fistula and inanition with slow downhill postoperative course, 5; (2) heavy secondary peritoneal infection with shorter postoperative course, 7; (3) generalized tuberculosis, 4; (4) intestinal obstruction, 2; (5) primary renal tuberculosis, uremia, 1; (6) shock, 1; and (7) pulmonary embolus, 1.

TABLE 11—*Types of Operations and Absence of Pulmonary Activity in the Two Groups*

	Living After Leaving Hospital, 17	Died After Leaving Hospital, 18
Exploratory laparotomy	15	5
Complete pelvic operation	20	7
No operation	2	2
Other operations	10	1
Pulmonary activity	10	10
Lungs clear	37	7
Questionable activity	2	1

It is realized that the first three causes of death overlap to a great extent, particularly in that in many of the patients with a secondarily infected type drainage was instituted judiciously with immediate improvement, the patients dying later of fistula formation and inanition.

The five patients not operated on died of (1) generalized tuberculosis, 3; (2) intestinal hemorrhage, 1; (3) primary renal and generalized tuberculosis, 1.

Table 10 shows the type of disease, type of operation and cause of death in the 26 patients who died in the hospital.

We have succeeded in tracing 65 of 161 patients discharged from the hospital. Eighteen of these died in from one month to twenty-seven years after leaving the hospital. Most of the deaths were from pulmonary tuberculosis within the first five years after discharge. The patient who lived for twenty-seven years died of intestinal obstruction. The patients who died of pulmonary tuberculosis within the first year after discharge were as a rule those who had showed activity of the pulmonary process while in the hospital.

TABLE 12—Individual Results in Patients Still Living

Number	Pulmonary Activity	Type of Peritoneal Disease	Operation	Well After
U-4880	No	Chronic adhesive fistula	For cure of fistula	3 months
U-2824	No	Encapsulated ascites	Posterior colpotomy complete pelvic	2 months
U-2743	Yes	Disseminated ascites pelvic masses adhesions	Exploratory laparotomy complete pelvic	2 years
U-1050	No	Encapsulated ascites	Exploratory laparotomy	1½ years
M-41744	Yes	Ascites	None	8 years
30637	Yes	Disseminated ascites	Exploratory laparotomy	2 years
30091	No	Pelvic masses	Complete pelvic	3 years
30029	Yes	Disseminated	Complete pelvic	1 year
29951	No	Pelvic masses encapsulated ascites	Complete pelvic	1 year
29193	Yes	Healing adhesive	For cure of fistula	4 years
28863	Yes	Disseminated ascites	None	Not well 3 years
28657	No	Disseminated ascites	Exploratory laparotomy	4 years
28449	No	Adhesive chronic	Conservative pelvic	3 years
28032	Yes	Adhesive chronic	Complete pelvic	6 years
28029	No	Disseminated ascites	Exploratory laparotomy	5 years
27715	Yes	Pelvic masses chronic adhesive	Complete pelvic	5 years
25564	No	Disseminated	Exploratory laparotomy	7 years
24949	No	Encapsulated fluid adhesive	Posterior colpotomy complete pelvic	7 years
24490	No	Disseminated ascites adnexal masses	Exploratory laparotomy conservative pelvic	9 yr 3 mo
24122	No	Disseminated ascites	Exploratory laparotomy	9 years
23874	No	Disseminated ascites	Exploratory laparotomy partial salpingectomy	9 years
23729	No	Disseminated ascites	Complete pelvic	1 year
22098	No	Pelvic abscess large pelvic masses	Posterior colpotomy complete pelvic	12 years
21971	No	Disseminated ascites	Exploratory laparotomy	11 years
21933	No	Disseminated	Complete pelvic	12 years
18367	No	Disseminated ascites	Exploratory laparotomy	17 years
19326	No	Disseminated ascites	Exploratory laparotomy	14 years
19170	Yes	Encapsulated ascites	Conservative pelvic	14 years
17447	No	Tubes closed localized	Plastic on uterine cornu	Not well 6 months
15161	No	Disseminated large pelvic masses	Complete pelvic	19 years
14400	Yes	Chronic adhesive	Complete pelvic	1 year
1247	?	Disseminated ascites	Exploratory laparotomy	1 year
10437	No	Encapsulated fluid	Exploratory laparotomy	24 years
949	No	Disseminated ascites	Exploratory laparotomy	20 years
973	No	Pelvic masses pus in pelvis	Complete pelvic	2 years
800	No	Pelvic masses ascites	Complete pelvic	2 years
879	No	Disseminated ascites	Conservative pelvic complete pelvic	2 years
744	?	Disseminated ascites	Exploratory laparotomy	25 years
700	No	Disseminated ascites	Right salpingectomy	27 years
647	No	Disseminated	Conservative pelvic	31 years
627	No	Disseminated ascites	Complete pelvic	33 years
627	No	Adhesive	Complete pelvic	2 years
598	No	Disseminated ascites	Conservative pelvic	33 years
4	No	Disseminated ascites	Exploratory laparotomy	15 years
330	No	Masses in pelvis	Complete pelvic	5 years
257	No	Disseminated	Complete pelvic	5 years
2	No	Ascites pus in abdomen	Exploratory laparotomy	5 years



Forty-seven are living, and it is a fact worth noting that these patients almost uniformly report themselves as very well, no matter what the operation or type of disease. There have been no pregnancies in any of the patients whom we have been able to follow up.

The types of operations performed and the presence or absence of pulmonary activity in these two groups are summarized in table 11.

It will be seen from table 11 that 11 of the 18 patients who have died since leaving the hospital had definite or questionable pulmonary

TABLE 13—*Individual Results in Patients Who Died After Leaving Hospital*

Num- ber	Pulmo- nary Activity	Type of Peritoneal Disease	Operation	Cause of Death	After Dis- charge
29903	No	Disseminated, ascites upper part of abdomen	Exploratory laparotomy	Pulmonary tuber- culosis	1 yr
28806	Yes	Masses in pelvis ascites	None	General tuber- culosis	1 day
28797	Yes	Ascites lung and spine	None	General tuber- culosis	1 yr
26115	Yes	Fresh adhesive	Exploratory laparotomy	Pulmonary tuber- culosis	1 yr
26232	No	Chronic adhesive	Conservative pelvic	?	2 yrs
26209	No	Disseminated, ascites	Complete pelvic	?	1 mo
20333	Yes	Chronic adhesive, enlarged glands	Complete pelvic	?	?
24196	No	Disseminated, ascites	Exploratory laparotomy	?	4 yrs
21213	No	Chronic adhesive	Conservative pelvic	?	9 yrs
18217	Yes	Disseminated ascitic, pelvic masses	Exploratory laparotomy complete pelvic	Pulmonary tuber- culosis	4 yrs
11872	Yes	Pelvic masses fistula to bowel	Complete pelvic	?	?
13616	?	Fresh adhesive	Exploratory laparotomy	?	10 yrs
10392	Yes	Fresh adhesive	Complete pelvic	?	?
9519	Yes	Disseminated, ascites	Conservative pelvic	Pulmonary tuber- culosis	4 yrs
8809	Yes	Disseminated	Complete pelvic	?	?
6597	No	Disseminated, ascites	Left salpingectomy	Embolus after cholecystostomy	4 yrs
7907	No	Disseminated, ascites upper part of abdomen	Exploratory laparotomy	Intestinal obstruction	27 yrs
1739	Yes	Disseminated	Complete pelvic	Pulmonary tuber- culosis	1 yr

activity during their stay in the hospital, while only 12 of the 47 who are still living showed such activity.

Tables 12 and 13 present the individual results in these two groups of cases, showing at the same time the type of disease, the type of operation and the presence or absence of pulmonary activity.

#### CONCLUSIONS

In thus reviewing the statistical data of 187 patients with tuberculous peritonitis treated on the Gynecological Service of the John Hopkins Hospital, we have been able to reach the following conclusions:

- 1 The incidence has been small as compared with other statistics gathered from the literature.

- 2 The incidence has been more than twice as great among colored as among white patients.

3 There has been a decided decline in incidence during the period under consideration, from 1889 to 1927. This has been more uniform and striking in the white than in the colored race.

4 The disease is most common among young adults in the second, third and fourth decades of life.

5 There is no striking etiologic relationship between pregnancy and tuberculous peritonitis to be derived from our series.

6 The disease may present all possible variations in the severity of its clinical manifestations but in the majority of cases it runs a chronic course.

7 Pain is the most constant of all symptoms; ascites the most suggestive of all signs.

8 Active pulmonary tuberculosis is frequently present before or after an anesthetic in tuberculous peritonitis (39 per cent). Healed lesions of some extent are found particularly frequently since the advent of the roentgen ray as a diagnostic adjunct.

9 Active pulmonary involvement while in the hospital seriously affects the prognosis during the first five years after operation.

10 All of the tubes removed from patients with tuberculous peritonitis showed tuberculosis of the endosalpinx. Individual records support the contention that in the adult female the tubes are usually the primary abdominal focus of the peritoneal disease.

11 Tuberculosis of the endometrium occurred in about half of the cases in which it was examined but these as a rule were cases in which the disease was very extensive. Leukorrhea and amenorrhea are frequently associated with involvement of the endometrium but other causes such as extensive pulmonary disease or destruction of the ovaries are often present to account for the amenorrhea.

12 In the ascitic disseminated type of tuberculous peritonitis the patient is usually treated by exploratory laparotomy with evacuation of the fluid. Patients with this type of the disease usually die only of pulmonary involvement. With treatment in a good sanatorium the prognosis is excellent.

13 Patients with the adhesive cystic variety and pelvic masses are treated by removal of the diseased adnexae if possible, if not by exploratory laparotomy. The prognosis is good if the tubes are completely extirpated. Pulmonary tuberculosis is the menace in the cases of shorter duration.

14 In the secondarily infected group the patients are desperately ill. Surgical drainage is necessary to prolong life but is undertaken only as a last resort. Death follows later from fistulas with recurring empyema, pulmonary tuberculosis, or, being a major secondary

infection occurs usually only in those suffering from a very old, advanced peritoneal tuberculosis, and who would probably have already succumbed had there been much pulmonary activity

15 With the modern methods of anesthesia available, ethylene anesthesia should be employed in preference to ether, since pulmonary involvement has been shown to be a frequent factor

16 Operation should be followed by prolonged care in a sanatorium whenever possible

# A REVIEW OF UROLOGIC SURGERY

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ROCHESTER, MINN

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JEAN VERBRUGGE, M D

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LOS ANGELES

*(Concluded from p 342)*

## PROSTATE GLAND

*Hypertrophy*—Cambridge<sup>39</sup> stated that diabetes is particularly likely to develop during middle life. In a consecutive series of 850 cases 495 patients (58 per cent) were aged 41 years or more when sugar was discovered in the urine. Although hypertrophy of the prostate gland is a later manifestation of senescence than diabetes the approximation of the age of maximal onset makes it likely that one may be a complication of the other.

Many operations may be performed on patients with diabetes with no more than average risk, provided careful and proper preoperative and postoperative treatment is given. In order to prevent diabetic coma it is necessary to eliminate from the body, as completely as possible the source of the intermediate toxic products of metabolism giving rise to the condition, to increase the power of the tissues to store and utilize carbohydrate to a maximal extent and to supply easily digested and absorbed carbohydrate in sufficient quantity for the needs of the organism. The first requirement may be met by limiting the intake of protein and reducing the fat of the diet to a minimum. The second requirement is partially fulfilled at the same time for an excess of fat interferes with the storage and utilization of carbohydrate as well as being a potential source of toxic derivatives in diabetic patients. There is rarely sufficient improvement in carbohydrate storage and utilization brought about by dieting alone so that surgical treatment can be carried out and it is best to increase the patient's own powers artificially by giving insulin for a short period at least before and after the

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<sup>39</sup> Cambridge P I Protection in Diabetic P... I Urol 1 258 1929

operation With the help of insulin, it is possible to increase the storage capacity to any desired extent, and, if necessary, the whole of the energy requirements of the body can also be supplied temporarily by dextrose

Because many elderly diabetic patients are unusually fat, particular care must be taken in preparing them for operation A more prolonged period of careful dieting is required in order that the surplus fat may be removed and the weight may be reduced to at least the average level and preferably a little below The preparation of the patient with advanced diabetes, whose powers of carbohydrate, fat and protein metabolism are seriously deficient presents another difficult problem The patient must be regarded primarily as diabetic, and surgical procedures should not be undertaken until metabolic defects are thoroughly under control Usually two or three months' treatment with diet and insulin are required If he responds as he should to this treatment, there is a possibility that when the prostatectomy has been carried out successfully further improvement in metabolism may follow In one of Cammidge's cases the urine was kept sugar-free only by two daily doses of insulin of 20 units before the operation, but afterward it was found possible to reduce the dose gradually, and eventually the urine remained free from sugar, and the blood sugar ranged within normal limits, on the same diet without any insulin

There should be as brief a period of anesthesia as possible for operations on diabetic patients, and a two-stage operation with an interval between for recovery, is usually better than prostatectomy carried out at one time All anesthetics appear to diminish the alkalinity of the blood and to increase the sugar content, but there is a considerable difference in the extent of the changes produced by various anesthetics Chloroform is the most dangerous and should not be administered to such patients under any circumstances, ether is less harmful, but gas and oxygen or spinal anesthesia is best

A diet free from fat should be the invariable rule for at least three or four days after the operation When this dangerous period has been safely passed, greater variance may be permitted gradually although in the two-stage operation the amount of fat allowed in the interval should be strictly limited Carbohydrate, including the allowance of dextrose and fruit juice, should constitute the bulk of the diet and sufficient insulin should be given to maintain the blood sugar as nearly as possible within the normal range Acidosis discovered at an early stage can usually be controlled by making suitable alterations in the diet and cautiously administering alkalis by mouth It is generally better to commence the treatment with an intravenous injection of about 1 liter of warm, 10 per cent solution of dextrose given at a rate not exceeding from 200 to 300 cc each hour with 10 units of insulin sub-

cutaneously at once and at hourly intervals afterward until from 30 to 40 units have been administered

Devoting a few days or weeks to the preparation of a diabetic patient may ultimately make the difference between success and failure of the operation

Harris<sup>40</sup> has successfully performed his operation of complete closure without mortality in 84 of 92 consecutive prostatectomies for benign prostatic hypertrophy during a period of eighteen months

Harris used the following operative technic. A transverse incision from 5 to 7.5 cm long is made through the skin and fat 2.5 cm above the top of the symphysis pubis or about 3.5 cm above it only preliminary cystotomy is intended. The bladder is picked up with tissue forceps and opened and the peritoneum is reflected to its topmost part. The intra-urethral method of bimanual enucleation of the prostate gland is carried out and the gland is removed. Electrically-lighted bladder retractors are then inserted.

For retormation of the floor of the prostatic urethra a triangular flap of trigonal tissue is drawn down into the prostatic cavity and sutured to the posterior portion of the floor of the cavity as close as possible to and often picking up the torn edge of the prostatic urethra. A long pair of angular ring forceps is passed into the prostatic cavity to pick up the capsule at a point low on the posterior wall. With slight traction this is easily brought into view in most cases. A special needle is then passed deeply from above downward by means of a special needle holder, this enters the mucosa from 0.83 to 1.25 cm behind the prostatic rim and emerges deep in the prostatic cavity having either passed deeply to or transversed the tissue previously caught up by the ring forceps. The needle is then rotated upward by compression of the handle of the holder and emerges from the prostatic cavity into the bladder where a loop of catgut is placed in its slot by a special carrier. The spring is released and the needle retraces its track armed with the catgut. When this is tied a tongue-shaped flap of trigone is drawn down into the cavity the horizontal trigonal shelf being converted into a more or less vertical gutter.

For obliteration of the prostatic cavity two or three anterior transverse sutures of catgut are used traversing the prostatic cavity deeply from side to side. The first stitch passes deeply in the plane of a tangent to the foremost part of the prostatic ring penetrating the mucosa well out on each side taking as large a bite as the needle will hold and just skimming the floor of the prostatic cavity in the depths. This stitch is drawn tight and tied and its ends held taut while are

<sup>40</sup> Harris, S. H. Suprapubic Prostatectomy with Closure of Urethra. *J. Urol.* 1: 285, 1929.

second stitch is passed parallel to the first and about 1 cm farther back. A rubber catheter is then passed through the urethra into the bladder. The tip of the catheter is drawn up out of the bladder and its eye transfixed by a needle armed with a length of silkworm gut. This is used to tether the catheter to a glass rod laid along the front of the abdominal incision.

To close the incision in the bladder one suture only of number 3 plain catgut is generally used. It is of an extended figure-8 type with three loops. The needle first penetrates the aponeurosis and rectus muscle at the lower angle of the wound on the left side, crosses over to the opposite side and picks up a good bite of the muscle of the bladder about 2 cm external to the incision in the bladder. It then crosses back to the left side, and, returning to the right, picks up the edges of the incision, either just missing or just picking up the mucosa. It is then again carried back and picks up the muscle of the bladder on the left side about 2 cm external to the incision. Finally, it crosses again to the right and penetrates the rectus muscle and aponeurosis from within outward. When this suture is drawn tight the cut edges of the incision of the bladder are brought into close apposition and inverted 2 cm into the bladder, the muscular wall of which is fixed snugly to the abdominal parietes, so that the space of Retzius is obliterated and dead spaces are not left.

Convalescence is simple and the patient suffers little disturbance. Irrigation of the bladder is not practiced, only enough fluid being injected, when necessary, to free the catheter of clots. The catheter is retained in position until the tenth day. Usually there is no leakage of urine through the wound during this period, and the original dressings remain until the fifth day.

Wildbolz<sup>41</sup> described his technic of perineal prostatectomy, which differs from other perineal methods by the preservation of the external sphincter. Only a minimal part of the membranous urethra is exposed and the prostatic capsule is opened about 1 to 2 cm below the apex of the prostate gland. Suturing between the bladder and urethra, as well as the closing of the prostatic capsule, reestablishes the integrity of all the structures. Wildbolz did not observe continuous incontinence in 340 perineal prostatectomies, and only in 3.5 per cent was there any weakness of the bladder for a period of weeks or months. There were nine rectal fistulas, which closed spontaneously or by secondary operation. The mortality rate was 6 per cent, 74 per cent of the operative wounds healed within fourteen days and 17 per cent within three weeks.

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<sup>41</sup> Wildbolz, H. Die Technik der perinealen Prostatektomie und ihre klinischen Erfolge. VIII. Tagung der Deutschen Gesellschaft für Urologie, Ztschr f urol Chir 26:312, 1929.

[Compilers Note—Wildbolz is a strong advocate of perineal prostatectomy. His technic differs somewhat from Young's in the manner of dealing with the membranous urethra and of opening the prostatic capsule. Preservation of the external sphincter is his chief aim. Wildbolz gives as one of his main reasons for choosing the perineal route the excellent opportunity afforded for radical prostatectomy when malignancy is unexpectedly encountered in a gland which has been diagnosed as benign.]

Chute<sup>42</sup> stated that he prefers the two-stage suprapubic prostatectomy in the majority of cases of prostatic obstruction, but expressed the belief that the perineal route is the best for removing small fibrous prostate glands, most malignant glands, and a large proportion of hypertrophic glands in obese men.

At the time of performing the first stage, Chute usually performs double bilateral vasotomy. The second stage is performed at varying periods of from ten days to many weeks or even months later, depending mainly on the condition of the patient's kidneys and heart. Spinal anesthesia is employed for the second stage in most cases because of its safety.

The two-stage operation has three definite advantages over the one-stage suprapubic prostatectomy, especially in case of a poor risk. It affords better opportunity for preparation of the patient as regards the kidneys, it diminishes the amount of hemorrhage encountered at the time of enucleation, and it minimizes the sepsis and sloughing of the suprapubic wound and perivesical tissues. Preliminary drainage afforded by the two-stage operation not only permits the kidneys that have been affected by back-pressure to readjust themselves to proper function but lessens the congestion of the prostate gland and the outlet of the bladder in this way diminishing the tendency to bleeding at the time the gland is enucleated.

*Carcinoma*—Zinner<sup>43</sup> stated that with the characteristic rectal signs of prostatic carcinoma a distinction must be made from prostatic calculi by roentgenograms and from prostatitis by the intramuscular injections of a nonspecific milk preparation (sterile milk in ampules). If metastasis is not present the relation of the carcinoma to the rectal mucous membrane should be determined. If the latter is movable a radical operation may be undertaken. Carrying out this principle by means of complete prostatectomy and resection of the trigone he obtained good

42. Chute, A. L. Certain Advantages of the Two Stage Suprapubic Prostatectomy. *New England J. Med.* **200** 1075 1929.

43. Zinner, A. Beitrag zur operativen Therapie des Prostatacarcinoms. VIII. Tagung der Deutschen Gesellschaft zur Urologie. Zürich 1929. *Chir.* **26** 312 1929.



results in 3 cases. One patient was free from recurrences for four years, then death occurred from intercurrent disease. Another patient lived two and a half years without symptoms, and a third patient lived one and a half years with local recurrence.

Cases in which the rectal mucous membrane is fixed are not amenable to radical operation. In such cases roentgen rays or radium may be tried. Results from the latter have not been satisfactory. In only a fourth of the cases is the length of life prolonged.

Hunt<sup>44</sup> stated that carcinoma within the substance of the prostate gland is difficult to recognize, and it may be suspected on clinical examination only when it is near the capsule and urethral surfaces of the gland. Since all prostatic tissue is not removed in the operation for benign prostatic disease, it is possible for an entirely benign adenomatous process to be removed, leaving tissue in which carcinoma may develop subsequently.

Four cases are cited by Hunt in which carcinoma developed in the prostate gland after prostatectomy. In one case carcinoma developed eighteen years after prostatectomy for benign adenomatous hypertrophy, and the time between prostatectomy and necropsy was sufficiently long to eliminate the possibility of malignant tissue having been left behind at the time of prostatectomy. Reexamination of the specimen from the first operation, which had been preserved for eighteen years, showed it to be entirely benign. In a second case evidence of malignancy appeared two years after prostatectomy. Although the final microscopic sections in this case were not available, digital examination and the roentgenographic demonstration of metastasis to the bones of the pelvis and lumbar spine indicated the presence of malignancy. In the third case evidence of malignancy appeared about six months after prostatectomy. One patient died several days after removal of the prostate gland, and at necropsy a small carcinoma was found in the prostatic capsule. In this instance definitely encapsulated, benign adenomatous hypertrophied tissue was present in association with carcinoma. The gland was readily enucleated, and on careful section failed to show any evidence of a malignant condition.

In these four cases only the first properly may be considered as a true example of a malignant growth developing subsequent to prostatectomy for benign disease. The others are probably cases in which the malignant condition was present but was not removed at the time of prostatectomy.

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44 Hunt, F. C. Carcinoma of the Prostate Gland and Prostatic Capsule Developing Subsequent to Prostatectomy for Benign Prostatic Hypertrophy, *J Urol* 22: 351, 1929.

Bugbee<sup>45</sup> reported 6 cases in which small carcinomas were found in the lateral and median lobes of the prostate gland and in which the condition was diagnosed only on microscopic section after removal. A careful examination of all prostate glands may make it possible to detect small suspicious areas, indicating prostatectomy in some cases in which otherwise palliative measures might be continued. Retention which occurs suddenly in the presence of comparatively mild urinary symptoms may suggest malignancy. Prostatectomy may be carried out as easily in these cases as in simple hypertrophy. Preliminary suprapubic drainage, allowing edema and infection to subside, is an advantage. There is evidence that the small amount of trauma incident to the removal of these prostate glands has caused a squeezing out of carcinoma cells into the lymphatics and a consequent spread of disease.

*Infections*—Mitchell and Von Lackum<sup>46</sup> stated that it is now estimated that approximately 60 per cent of the cases of prostatitis are non-gonorrheal in origin.

In male patients aged 50 years or more, with the usual degree of senile prostatic enlargement, eight or ten pus cells in each high-power microscopic field may be present but are of no clinical significance. Unsatisfactory results of radical treatment of hypertrophy of the prostate gland and associated inflammatory prostatic bar obstruction have shown that, even in advanced years, prostatic infection sometimes has a more important bearing on urinary obstruction than adenomatous enlargement of the gland. Frequently in elderly men, with nocturia as the only urinary disturbance, a few prostatic massages or the passage of a moderately sized gum elastic catheter two or three times is sufficient to give relief. This indicates that the symptoms of obstruction are of inflammatory origin, although symptomless senile enlargement may also be present. The presence of small clumps of pus cells is practically always diagnostic of prostatic infection. Several provocative treatments may be required to bring out the severity of latent prostatic infections.

In a study of cultures of the expressed prostatic secretions of 405 cases, Von Lackum found that 141 (35.25 per cent) were sterile. The size of the prostate gland and the degree of infection were not correlated, often a small apparently insignificant gland was found to carry the highest degree of infection. In the absence of pus cells there may be organisms which are active or potentially virulent.

The diagnosis of prostatitis should not be made by digital examination alone as it is not an infallible index of the degree of infection. In

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45. Bugbee H. G. Cases of Un-suspected Carcinoma of the Prostate Discovered on Microscopic Section. *J. Urol.* **22**: 353, 1929.

46. Mitchell John and Von Lackum W. H. Chronic Prostatitis and Vesiculitis. Physical and Microscopic Data. *Bull. J. Urol.* **1**: 277, 1929.

estimating the consistence of the gland, care must be exercised not to mistake superficial edema of the structures between the examining finger and the prostate gland itself for abnormal softness of the tissue of the gland. Sometimes in prostate glands of small size there is the impression that the capsule is under tension which is usually significant of definite prostatic infection. The *globus major* is thickened in most cases in which prostatitis is present. This thickening and also a distinctive tenderness may be recognized by palpation.

The seminal vesicles may be tender, enlarged, thickened and indurated, or atonicity alone may be the only palpable alteration. Along with these changes, the ampulla of the vas deferens, which normally is not palpable, may be thickened and readily palpated. The normal secretion of the seminal vesicles contains globules, and by means of them it is distinguishable macroscopically from normal prostatic secretion. The chief pathologic contents are pus cells, degenerated cells and often oil-like globules in fair number.

*Stones*—Rabinovič<sup>47</sup> cited 2 cases of prostatic stones. In 1 case there were ninety-six stones, lying within the gland. In the second case there were three stones in the upper part of the gland, this resulted in enlargement toward the bladder giving cystoscopically, the picture of tumor.

Rabinovič concluded that gonorrhea as an etiologic factor may be of significance. Urinary fistulas are seldom associated with prostatic calculi. In doubtful cases in which roentgenogram of the bladder shows a shadow similar to stone but not in the usual situation, differentiation must be made of a stone in a vesical diverticulum, stone in the intramural portion of the ureter, and a stone in the prostate gland. Stone in a vesical diverticulum may be recognized by means of the cystoscope and cystography. Ureteral stone may be identified by ureteral catheterization. Prostatic stone is diagnosed by excluding the foregoing conditions. The technic of the operation depends on the position of the stones.

#### EPIDIDYMISS, SEMINAL VESICLES AND TESTES

*Tumor*—Dean<sup>48</sup> made a statistical study of 124 patients with teratoid tumors of the testis treated with external irradiation by means of high-voltage roentgen and radium packs.

It was noted that direct trauma preceded the formation of tumor in 11 per cent of the cases. Incomplete descent of the testis predisposes to malignant degeneration whether the testis is in the abdomen or in

47 Rabinovic, M. Intraglandulare Prostatsteine, Sibirsk Arch teor i klin Med 2 786, 1927, abstr, Ztschr f urol Chir 26 231, 1929.

48 Dean A. L., Jr. The Treatment of Teratoid Tumors of the Testis with Radium and the Roentgen Ray, J Urol 21 83, 1929.

the inguinal canal With the use of Ewing's classification, the histologic diagnoses were as follows: embryonal carcinoma, 40 per cent, teratoma 18 per cent, sarcoma, 9 per cent, cellular adenocarcinoma 5 per cent, mixed teratoma, 2 per cent, adult cystic teratoma, 0.82 per cent, adult leiomyoma 0.82 per cent, orchidectomy without histologic examination, 12 per cent, no operation, 11 per cent

The first symptom in 92 per cent of the cases was a painless swelling of the testis Other symptoms were loss of weight in 57 per cent of the cases, cramplike pain in the lower part of the abdomen in 19 per cent, pain in the back in 17 per cent, indigestion in 14 per cent, loss of strength in 14 per cent, tumor in the lower part of the abdomen in 12 per cent, constipation in 9 per cent, tenderness of testis in 8 per cent, swelling of lower limb in 5 per cent, mass in the epigastrium in 4 per cent, swelling in the left side of the neck in 4 per cent and vomiting in 2 per cent Metastasis occurred in the abdomen of the affected side in 69 per cent of the cases, in the left supraclavicular fossa in 9 per cent in the lungs in 8 per cent, in the epigastrium in 7 per cent in the mediastinum in 3 per cent in the liver in 2 per cent in the kidney in 1 per cent in the spleen in 0.6 per cent, in the breast of the opposite side in 0.6 per cent and in the brain in 0.6 per cent

Dean considered it important that in the examination of intrascrotal tumors the possibility of teratoma should be kept in mind Careful palpation of the abdomen of the same side is essential

In the treatment of most teratoid tumors of the testis, operative procedures alone offer but little hope of cure Because of the undifferentiated nature of their cellular structures, these tumors are especially amenable to irradiation Conversely, the tumors most lacking in malignant qualities are the least radiosensitive

Thirteen patients in whom the condition was considered as primarily operable were not operated on and there was no metastasis Ten (79 per cent) are living One patient died about eighteen months later two patients were not traced Two of the patients in the group refused operation and are living and well after treatment by external irradiation

In 3 cases local recurrence followed orchidectomy In 1 case operation was performed and irradiation was used in all others All the patients are living and free from disease 1 patient for three years and six months 1 for four years and eight months and 1 for ten years and six months

There were 81 patients who after orchidectomy had inoperable local recurrences, metastasis or both Twenty-four (30 per cent) are known to be living, 56 (70 per cent) are dead

Eleven patients were observed soon after orchidectomy There was no demonstrable recurrence or metastasis Prophylactic irradiation was given Eight patients (72 per cent) are living

Dean concluded that when a patient has a teratoid tumor of the testis and metastasis cannot be found, the treatment of choice consists of thorough irradiation of the testis and abdomen of the same side, followed in from four to six weeks by orchidectomy. Several courses of irradiation should follow at as short intervals as the toleration of the patient will permit. An attempt should not be made to remove growths that have metastasized from a malignant testicular tumor. Maximal irradiation by means of the radium pack and high voltage roentgen rays offers a greater chance for permanent relief.

*Tuberculosis*—Ullmann<sup>49</sup> considered 43 cases in which treatment by roentgen ray had a beneficial effect in genital tuberculosis in males. In most cases local signs such as swelling and infiltration, diminished within a short time. There was also improvement in the tuberculous infection of the prostate gland, seminal vesicles and scrotum. Tuberculosis of one testis was prevented from spreading to the other by roentgen irradiation of the normal organ. Occasionally abscess formed following radiotherapy. In the etiology of epididymal tuberculosis trauma appeared to be a significant factor. Beneficial results were obtained by repeated doses of roentgen rays, with long intervals between. Radiotherapy is not a substitute for operation, but it is a good adjunct even in cases in which complete removal is not possible.

[Compilers' Note—This report is one of the most sanguine concerning the value of roentgen treatment in genital tuberculosis. Most American writers group this form of treatment with institutional hygienic treatment, heliotherapy and ultraviolet-ray treatment. They speak of radiotherapy as causing cicatricial encapsulation of the tuberculous focus and as being accompanied by marked atrophy of the seminiferous tubules of the testis. When controlled microscopically, which has seldom been done, the tuberculous focus is found to be not healed but merely encapsulated by scar tissue. However, this in itself may have an ameliorative effect on the process and result in improvement in the patient's general health.]

Operative attack, although the subject of sharp controversy as to type, is generally the method of choice among urologists. Many observers believe that the removal of the tuberculous epididymis or kidney will be attended by subsidence of activity of the tuberculous process in the prostate gland and seminal vesicles. Young, on the other hand takes a radical stand to the contrary, believing that the prostate gland and vesicles are the primary focus and should be treated early and directly by complete eradication.

49 Ullmann, K. Erfahrungen über Röntgentherapie bei der männlichen Genitaltuberkulose, *Monatschr f Harnkrankh u sexuelle Hyg* **1** 161, 227, 257, 289, 1928, **2** 3, 65, 103, 1928, abstr. *Ztschr f urol Chir* **26** 229, 1929.

Just what will be the development in the treatment of patients with genital tuberculosis by means of the roentgen rays is a matter of conjecture. As Ullmann cautiously pointed out, it is at present hardly a substitute for operation but may be a valuable adjunct. One would anticipate marked deleterious effects on the endocrine function of the testes, a disadvantage which does not necessarily accompany surgical measures.]

*Infection*—Pugh<sup>50</sup> stated that seminal vesiculitis is a common disease. In the acute stage its symptoms are markedly similar to those of acute appendicitis and often lead to incorrect diagnosis and appendectomy. If there are symptoms of acute appendicitis Pugh considers it important to obtain the patient's venereal or urologic history, as well as to make a rectal examination, before contemplating removal of the appendix.

#### URETHRA

*Rupture*—Wheeler<sup>51</sup> reviewed 6 cases of traumatic stricture of the urethra, and observed that rupture of the urethra occurs more frequently in the bulbous portion than in the membranous urethra. Ruptures in the bulbous urethra are more prone to develop intractable stricture than are those in the membranous portion. When rupture is in front of the triangular ligament, perineal hematoma almost invariably occurs. There is intense and ineffectual desire to urinate with severe local pain. Extravasation of the urine is prevented by a reflex spasm of the compressor urethra muscle for several hours. The amount of bleeding from the meatus after the accident is often in inverse proportion to the amount of injury to the urethra. After the partial division, hemorrhage is likely to be more profuse and continuous, when the division is complete the retraction of the part favors hemostasis, and the line of least resistance for the escape of blood is into the cellular tissues. In this way the gravest rupture is accompanied by the large hematoma. The exact site of the rupture is not always easily ascertained. If the pelvis is broken the rupture is more likely to take place above the triangular ligament in the region of the apex of the prostate gland. In traumatic cases of rupture of the urethra urine is ordinarily not infected at the time of injury and the prognosis is consequently better than in extravasation of urine behind a long-standing stricture.

Early operation is important. Wheeler uses the following technique. The patient is prepared in both the suprapubic and perineal regions. The anterior urethra is washed out but no attempt is made to pass a catheter at this stage unless there is doubt about the diagnosis. Gas is the anesthesia of choice. Perineal section is done and the bladder is opened suprapubically. At the same time with the finger as a guide

<sup>50</sup> Pugh W. S. Seminal Vesiculitis or Appendicitis? *J Urol* **22** 313 1929

<sup>51</sup> Wheeler W. I. deC. Traumatic Rupture of the Urethra. *Proc Ro Soc Med* **22** 469 1929

a catheter is passed in the retrograde fashion and held in position by an assistant. Clots are removed through the perineal incision, torn muscles and brushed bits of tissue are excised by sharp dissection and bleeding is controlled. A rubber catheter is passed by way of the meatus into the perineal wound and secured to the instrument which has been passed in the retrograde fashion into the bladder. The catheter is pulled into the bladder. A long thread is attached to the eye-end of the catheter and brought out through the suprapubic drainage tube. The urethra is then sutured over the catheter and perineal wound, and closed with a small superficial drain. The catheter is changed every fourth day by fastening the eye-end of a new catheter into the outer end of the one in use at the time, and then by traction on the thread, the new catheter is drawn into the urethra while the used one is withdrawn through the suprapubic incision. At the end of two weeks the retained catheter and suprapubic drain are discarded, and instruments are not passed until both the perineal and suprapubic wounds have healed completely. The patient should have monthly examinations for a year after operation to prevent the formation of a progressive stricture.

In traumatic stricture, as distinct from gonorrheal stricture, the narrowing is extrinsic as well as intrinsic, there is fibrosis of the deep tissues of the perineum surrounding the urethra besides the irregular healing of the divided ends. If the perineal wound, in the absence of an indwelling catheter, is allowed to remain open and heal by granulation, the amount of scar tissue is greatly increased. It is Wheeler's belief that by employing the retention catheter for two weeks and avoiding perineal drainage, the patient is more comfortable, the scar in the perineum is reduced to a minimum, subsequent instrumentation is simplified and convalescence is hastened.

Young<sup>52</sup> reported 9 cases of fracture of the pelvis complicated by rupture of the urethra which illustrate the importance of early operation and accurate repair of the urethral defect in such cases. In cases in which operation was delayed, it was necessary to carry out extensive secondary operations to cure fistulas, and to relieve patients of incontinence of urine. If operation was performed immediately, excellent results were obtained without serious complications. Young expressed the belief that careful investigation of the urinary tract should be made in all cases of fracture of the pelvis. If the posterior urethra is ruptured, the safer procedure is to carry out anastomosis immediately if the rupture is complete, as was done in one of Young's cases, to close the defect over a catheter, as was done in a second case. With perineal and suprapubic drainage, the danger of infection is avoided and excellent results are obtained.

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52 Young, H. H. Treatment of Complete Rupture of the Posterior Urethra, Recent or Ancient by Anastomosis, *J. Urol.* 21: 417, 1929.

[Compilers' Note—The surgical principles outlined by Wheeler in dealing with traumatic rupture of the urethra are worthy of note. Passing the catheter through a suprapubic cystotomy opening simplifies the effort to recognize at once the proximal portion of the torn urethra. A second catheter passed through the meatus and on into the bladder with the aid of the instrument passed retrograde from above serves as a splint over which the torn urethral ends may be accurately sutured. Frequent change of this catheter in the manner outlined by Wheeler serves to prevent pressure necrosis, whereas suprapubic drainage favors healing with minimal infection and allows the perineal wound to be healed with the least degree of scar formation and the least opportunity for the development of fistulas. External urethrotomy alone is often a difficult procedure when the operator dissects slowly in a cicatricial, traumatized and bloody field in an effort to secure the urethral ends. Young likewise emphasized the value of suprapubic and perineal drainage in avoiding infection. The same principle is now being applied frequently in promoting the healing of repaired vesicovaginal and other fistulas of the lower portion of the urinary tract.]

*Verumontanum Changes*—Begg<sup>53</sup> stated that pathologic changes in the verumontanum and the posterior urethra are common causes of urinary and sexual disturbances. It is suggested that the colliculus acts as a spout which, when thrust forward by the congestion and straightening of the ejaculatory ducts, directs the stream of semen along the axis of the urethra, the cavity of the bulb acting as a distributing reservoir. The tonus of the internal sphincter is aided in its function of preventing regurgitation by the congestion and erection of the ejaculatory ducts raising the prostate gland so as to occlude the supramontan urethra. The sinus pocularis is a vestigial remnant corresponding to the vagina in the female. It is not a functioning organ, but frequently acts as a trap for infection.

Granulomas due to infection are the most common pathologic conditions found in the verumontanum and may be eradicated by fulguration. The verumontanum in its relation to sexual life has been overemphasized. The organ does not contain erectile tissue and no special nerve-endings, being similar in this respect to the surrounding urethra.

#### ANESTHESIA

Grodinsky and Best<sup>54</sup> after a series of experiments in which cadavers were injected epidurally with methylene blue (methylthionine chloride U. S. P.), came to the following conclusions concerning sacral anesthesia:

53 Begg, R. C. The Verumontanum in Urinary and Sexual Disorders. *Br. J. Urol.* **1** 237, 1929.

54 Grodinsky, Manuel and Best, R. R. Sacral Anesthesia, an Experimental and Clinical Study. *J. Urol.* **22** 108, 1929.



An epidural injection of 20 cc of procaine solution is sufficient to anesthetize the fifth sacral nerve completely and the fourth partially, an injection of 30 cc will affect the fifth, fourth and third nerves completely, an injection of 40 cc will anesthetize the fifth, fourth and third nerves completely and the second and first less completely. When it is necessary to anesthetize the first two sacral nerves completely, more than 40 cc (50 to 75 cc) of procaine solution are needed. The preferable method of anesthetizing the first two sacral nerves is combining a smaller caudal injection (30 to 40 cc) with transsacral injection of the upper two sacral foramina.

In the experience of Grodinsky and Best, it was noted that 1 per cent or weaker solutions of procaine were practically as effective as the 2 per cent or stronger solutions and are to be preferred.

When excessive perineural fat and connective tissues are present it is difficult for aqueous solutions of dye or procaine to reach the bare nerves, and the use of some more penetrating anesthetic solutions is indicated.

[Compiler's Note—A 1 per cent solution of procaine has been found by the majority of anesthetists to be the most satisfactory. The average patient usually can stand 0.6 or 0.7 Gm of procaine in the sacral canal without having a reaction. Weaker solutions may be injected slowly, and reactions are more readily anticipated. The use of drugs, such as sodium bicarbonate, which is supposed to make the solutions more penetrating, is not satisfactory. Anesthetization of the lower three or four sacral nerves is generally sufficient for any manipulation of the neck of the bladder or for perineal or inguinal operations. Sacral anesthesia is especially satisfactory for urologic and rectal work and deserves to be much more extensively employed.]

Jeck<sup>55</sup> reported on more than 600 cases in which spinal anesthesia had been given since 1920 in the urologic service at Bellevue Hospital. An analysis of postoperative deaths in 536 of these cases showed the mortality to be about 4 per cent less with spinal anesthesia than with general anesthesia. In a series of more than 900 cases in which spinal anesthesia was given by Ehrlich, there were only 2 operative deaths, in neither instance could the death be attributed directly to the anesthetic.

Jeck's series of cases of spinal anesthesia included 21 cases in which nephrectomy was performed, in 14 of which it was for tuberculous kidneys. In 16 cases the anesthesia was perfect, in 2, the patients complained of slight pain, in 2, the patients complained only after the kidney had been removed, when it became necessary to administer general anesthesia in order to close the wound, and in 1 case a general anesthetic had to be given before the kidney was removed, after forty-five minutes of operating.

<sup>55</sup> Jeck, H. S. Nephrectomy under Spinal Anesthesia with Particular Reference to Nephrectomy in Renal Tuberculosis, *J. Urol.* **21** 61, 1929.

Jeck concluded that spinal anesthesia is successful for nephrectomy. It is especially indicated in renal tuberculosis when general anesthesia is frequently contraindicated because of pulmonary involvement. Nephrectomy is rendered comparatively easy to perform owing to the more complete relaxation with spinal than with general anesthesia. The patient's general appearance and behavior are good indications of his condition. During operation a fall in blood pressure, even when marked, is rarely a real danger signal. Procaine in the form of Pitkin's solution usually produces a more satisfactory anesthesia than procaine alone. Postoperative ileus does not frequently occur with spinal anesthesia.

[Compilers' Note—The application of spinal anesthesia in spite of the apprehension with which it was used when first introduced is rapidly becoming widespread. This has been especially true during the last three years. More careful control of the technic of administration, the use of purer drugs, and above all the ability to avoid or to control to a great degree the alarming vasomotor collapse by means of ephedrine have probably been the chief factors in bringing spinal anesthesia into its own.]

Henline's<sup>56</sup> choice of anesthesia in renal operations is combined paravertebral and local anesthesia. Preliminary medication is given of three doses of  $\frac{1}{8}$  grain (0.008 Gm.) of morphine sulphate in an ampule containing 2 cc. of a 50 per cent solution of magnesium sulphate in procaine at half-hour intervals before operation. One per cent solution of procaine, without epinephrine, has given the most satisfactory results. Injection of this solution is made below the transverse process of the vertebrae from the eighth thoracic to the second lumbar inclusive, the injection being made 5 cc. above and below each, except for the two lumbar nerves, when 10 cc. is used. This is supplemented by splanchnic analgesia and infiltration along the line of incision. More perfect anesthesia should be obtained by thus blocking each nerve twice along its course, using only a safe amount of procaine. Procaine is a safe anesthetic, provided the solution is injected slowly and not directly into the blood stream or spinal canal. The destruction of procaine in the liver is rapid, not cumulative and has no ill effects on the kidneys.

The technic of administration of a combined paravertebral and local anesthetic is more difficult for the surgeon but the advantages to the patient are sufficient to warrant its use. The advantages to the patient are fluids may be taken before, during and after the operation, the anesthesia persists for an average of three and a quarter hours after operation, less postoperative opiates are required and some patients are comfortable without any narcotic. Pulmonary complications are

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<sup>56</sup> Henline, R. B. A New Method of Paravertebral Anesthesia for Kidney Operations. Report of Thirty-Three Cases. *J. Urol.* **21**: 27, 1929.

diminished, abdominal distention is less common and severe, nausea and vomiting are rare, the mortality rate is lessened, and convalescence begins when the patient leaves the operating table. Because of the gentleness with which tissues must be handled, the operative procedures are carefully carried out. Relaxation of the tissues is complete. The kidney may be operated on regardless of any coexisting disease with less danger than under any other anesthetic. The method of anesthesia has been proved experimentally and clinically to be practical, successful anesthesia should be expected in at least 90 per cent of operations on the kidney. Pain is not experienced if the kidney is dissected gently from its bed, or if the renal pedicle is clamped and tied.

Heimann and Dózsa<sup>57</sup> reported the results of paravertebral anesthesia in 1,000 operations on the kidney and ureter. Transitory or permanent disadvantages which accompany inhalation, splanchnic or spinal anesthesia are not encountered in the use of paravertebral anesthesia. Low or high blood pressure, poor renal function, cardiac lesions or pulmonary involvement are not contraindications to its use.

A markedly neurotic and apprehensive patient should not be selected for paravertebral anesthesia. The evening before operation the patient is given 0.5 Gm. of veronal. Half an hour before he is taken to the operating room, he receives an injection of 0.02 Gm. of morphine sulphate. Procaine is the most desirable anesthetic, because it is the least toxic, most reliable and least expensive. In operations on the kidney and ureter, Hermann and Dózsa block from the eighth to the twelfth dorsal nerves, that is, the last five intercostal nerves and the first lumbar nerve.

[Compilers' Note—Regional anesthesia is in part rapidly replacing inhalation narcosis for operations on the kidney and ureter. Under the stimulus of Labat, who first popularized the method in America, paravertebral anesthesia has found acceptance in a number of clinics. Hermann and Dózsa emphasized its undisputed advantages. The technic is accompanied by excellent results and may be applied with entire satisfaction by those skilled in its use. The administration of paravertebral anesthesia, however, is painstaking and time-consuming. The recent renewed interest in spinal anesthesia, which seems to be sweeping over America, and the rapid and less difficult application in average hands, will probably cause this type of regional anesthesia to supplant paravertebral injection to some degree. Paravertebral anesthesia, when properly applied, will prove satisfactory, and it is not attended by the dangers, real or imagined, which cause the more conservative operators to approach spinal anesthesia with apprehension.]

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<sup>57</sup> Hermann, H. B., and Dózsa, Eugene. Paravertebral Anaesthesia in Urology, with a Report of Its Use in a Thousand Cases of the Kidney and Ureter, *Surg. Gynec. Obst.* 48:375, 1929.

## URINARY INFECTION

Campbell<sup>58</sup> considered some of the more common types of disease of the urinary tract in infants and children in which chronic pyuria is a predominant symptom. Age is not an etiologic factor in chronic pyuria. Urinary stasis encourages urinary infection, and may be due to organic obstruction or the result of neuromuscular disease of the urinary channels, especially the bladder and ureter. Organic obstruction of the urinary tract may be congenital or acquired. In a study of 2,420 necropsies on children at Bellevue Hospital, anomalies of the urinary tract were found in more than 7 per cent and in many of these the renal injury caused by congenital urinary obstruction was extreme. When disease is secondary to obstruction, the changes which occur above the point of obstruction are identical regardless of the character of the blockage.

The disease process in cases of obstruction and infection is one of chronic suppurative nephritis and is regularly observed in the study of sections of kidneys in cases of advanced obstruction. The usual route by which bacteria reach the urinary tract is from the blood stream through the kidneys, the origin of the bacteria is as a rule a focal infection of the upper respiratory tract, tonsils, sinuses or middle ears. The incidence of acute renal infections being preceded by acute exacerbations of such focal infections is so regular that their etiologic relationship is unquestioned. True cystitis or urethrocystitis in children in the absence of renal infection is undeniable and may cause persistent pyuria.

A tight prepuce or a tight meatus may cause obstruction, with dilatation of the entire urinary tract, as well as destruction of the kidneys. Congenital malformations of the valve of the posterior urethra are significant as the cause of urinary obstruction. These mucosal folds usually extend from some portion of the verumontanum to the lateral wall of the urethra. In some cases they are unilateral and in others they have no connection with the verumontanum but form an iris diaphragm which blocks the urethra. Injury to the urinary tract with renal destruction above the point of obstruction in these cases is usually extreme. The valves may be destroyed satisfactorily by transurethral instrumentation or by suprapubic approach. Obstruction at the renal outlet is usually the result of plugging of the opening by pelvic stone, blood clot or the debris of renal necrosis. Neuromuscular disturbances of the bladder are usually accompanied by pyuria. If there is chronic spasm of the vesical outlet urinary retention may be severe. In the latter stages when muscular paralysis has developed a large amount of residual urine will be found in the dilated atonic flabby bladder.

<sup>58</sup> Campbell M. F. Chronic Pyuria in Infancy and Childhood. *M. J. Rec.* 130:90, 1929.

A thorough urologic examination by the same technical methods as are employed with an adult is indicated when pyuria persists longer than four weeks, in spite of intensive systematic treatment. Such an examination includes careful urinalysis, the determination of the renal function by the phenolsulphonphthalein test, the observation of the chemical changes in the blood, roentgenograms of the urinary tract to rule out stone and spina bifida, cystography, cystoscopy, ureteral catheterization and divided renal functional tests for excretion of dye and urea, and pyelography when indicated. Children withstand urologic examination remarkably well and manifest fewer and less severe post-instrumental reactions than do adults. When completely performed these examinations will demonstrate the incorrectness of the diagnosis of chronic pyelitis on the basis of persistent pyuria and also the lesions of the urinary tract which may bring about chronic pyuria. Uncomplicated chronic inflammation of the renal pelvis does not exist, and pus originating in the upper part of the urinary tract is chiefly from the renal parenchyma. In many instances involvement of the upper part of the tract is slight or absent, whereas disease of the lower part of the urinary tract is marked.

Smith,<sup>59</sup> in reviewing fifty cases of renal infection, observed that peridental infections and disorders of the intestinal tract often precede or accompany the onset of pyelitis, but he was unable to determine the relationship between them. The infection often persists after the probable cause has been removed. Treatment used in one case is not always as effective in an apparently similar case. Pelvic lavage proved to be the best method of treatment, it will not clear up certain cases in which there is obstruction to drainage, but it is effective in cases in which only a minor obstruction is demonstrated. Vaccine and bacteriophage were found to have no appreciable value. Improvement in the patient's general resistance is important. In all cases in which the infection persists, a complete pyelographic and functional study of the kidneys should be instituted.

#### INFECTION OF THE BLOOD STREAM

Scott<sup>60</sup> has observed that transitory infection of the blood, or bacteremia, is more common in diseases of the genito-urinary tract than true septicemia. Of 82 patients, 62 per cent had infection of the blood stream after operation. The urethra was thought to be the portal of entry in 80 per cent of the cases. Seventy-seven per cent of the patients had bacillary infection, and 23 per cent coccal infection of the blood stream. Infection by colon bacillus occurred in 40 per

<sup>59</sup> Smith, G. G. Fifty Cases of Renal Infection, *New England J. Med.* **200** 867, 1929.

<sup>60</sup> Scott, W. W. Blood Stream Infections in Urology, a Report of Eighty-Two Cases, *J. Urol.* **21** 527, 1929.

cent of the cases Eighteen per cent of the patients died, in 74 per cent of these, infections were postoperative in origin and occurred in patients who were relatively poor operative risks

In cases of true septicemia attempts should be made to locate and eliminate when possible, the primary focus of infection In the presence of preoperative or postoperative sepsis whether or not cultures of the blood are positive, intravenous treatment may often be helpful Scott expressed the belief that every precaution should be taken to prevent the possibility of infection of the blood stream in urologic cases

[Compilers' Note—Urethral fever, after cystoscopic examination and after operation with chills and fever may serve to turn the tide against a patient who is already a poor risk The demonstration of positive cultures of the blood in such cases does much to clear up our understanding of the mechanism of such infections, as well as to emphasize their gravity The fact that 18 per cent of Scott's patients died post-operatively demonstrates the seriousness of the condition If, as this article seems to bring out, bacteremia is usually transient, then it is of the utmost importance to use intensive treatment to support the patient's resistance to the highest possible level This may be accomplished by stimulating the elimination, by supporting the cardiovascular system, by intravenous treatment perhaps and by establishing proper drainage of the urinary tract ]

#### URINARY EXTRAVASATION

Campbell<sup>61</sup> stated that periurethral phlegmon is a rapidly fulminating infection, with a mortality rate of approximately 50 per cent During the last fourteen years 135 patients with this disease have been admitted to Bellevue Hospital Early recognition of the lesion together with immediate institution of proper treatment is of prime importance

For anatomic reasons urinary extravasation is a disease peculiar to males Urethras scarred and ulcerated by infections past and present weakened and dilated by long-continued urinary back-pressure secondary to stricture offered the least resistance to infectious exacerbations

The prognosis depends on the virulence of the invading organisms, the site and duration of the disease and the degree of renal injury which has occurred The condition should be treated by radical surgical measures which are always emergency procedures Free drainage should be given the urinary bladder with wide incision and drainage of the involved tissues Genital cutaneous repair is rapid and satisfactory When stricture is demonstrated periodic dilatation with sounds should

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<sup>61</sup> Campbell M. F. Periurethral Phlegmon (Urinary Extravasation) *Surg. Gynec. Obst.* 45: 782, 1929

be used consistently after operation, as is customary for all strictures of the urethra. This treatment is the only prophylaxis against future phlegmons.

#### SPINA BIFIDA OCCULTA

Mertz and Smith<sup>62</sup> stated that it is not the bony defect itself which causes the remote nervous symptoms in spina bifida occulta, but also the nerve fibers of the cauda being adherent to the superficial structures or pressure on the cord at the point of the spinal defect. There may be a distinct meningocele protruding through the bony cleft, closure of the cleft by a tough membrane adherent to the skin, perforation of the membrane by a dense band attached to the subcutaneous tissue externally and compressing the structures of the cord internally, fatty tissue lying within the canal concealed by this membrane, bulging of the dura mater, exostosis within the canal compressing the cord structures, myofibrolipoma extending through the cleft into the bony canal, compressing the cord and its roots and degeneration of the cord tracts themselves. The presence of an added pathologic process explains why, in some case of spina bifida occulta, there are symptoms, and in another there are none. Mertz and Smith consider that this fact suggests the necessity for a readjustment of the point of view concerning the significance of the presence of spina bifida occulta, and will form a basis for its consideration in the future.

The urinary symptom most frequently observed in spina bifida occulta is urinary incontinence usually enuresis. Retention of urine in the bladder, the result of a detrusor muscle paralysis due to spina bifida occulta, with or without the loss of control of the sphincter of the bladder, has been reported.

Mertz and Smith urge the close cooperation of the urologist, the roentgenologist, and the neurologic surgeon in the detailed study of each case, as they believe that only in this way can the accurate relationship of cause and effect ultimately be determined.

#### PYELOGRAPHY

König<sup>63</sup> undertook experimental work, chiefly on dogs, to determine whether the "streak formation" often noted in pyelograms is due to the entrance of the contrast solution into the venous system of the kidney so-called pyelovenous reflux, or whether it enters the parenchyma by way of the tubules. The phenomenon is observed in the majority

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62 Mertz, H. O., and Smith, L. A. Spina Bifida Occulta, Its Relation to Dilatations of the Upper Urinary Tract and Urinary Infections in Childhood, *Radiology* **12** 193, 1929.

63 König, Ernst. Ueber die sogenannten Buschelbildung im Nierenrontgenbild, *Beitr. z. klin. Chir.* **144** 320, 1928.

of cases at the poles of the kidney, and less frequently in the median portion, either single or multiple. This streak formation was noted in one case, that of a boy aged 17, of 128 pyelograms examined.

After the bladder had been opened by the abdominal route, the catheters were introduced into both ureters to the renal pelvis, and the bladder and abdomen were closed. To eliminate all disturbance from motion during the exposure the animals were anesthetized and 2 cc of a contrast medium was injected. Roentgenograms were taken, and from 2 to 6 cc of additional fluid was then injected under rapid pressure. Roentgenograms were again taken. The animals were killed and the kidneys examined microscopically. From fifteen to thirty minutes usually elapsed between pyelography and examination of the kidneys.

As a result of these investigations, it was found that if an overfilling of the renal pelvis was produced by applying a rather high pressure, the entrance of the contrast solution into the uriniferous canals resulted, and in applying colored contrast solution under similar conditions, an experimental streak formation was observed. The streak formation consequently must be due to the entrance of the contrast medium into the uriniferous canals.

#### EMBOLISM

Thomas and Alyea<sup>64</sup> studied a group of cases in which the patients had died suddenly of pulmonary embolism after urologic operations and noted the following facts. The embolus nearly always originated in one of the femoral veins or one of its larger trunks. The thrombophlebitis of the pelvic veins, which occurred in almost every case, seldom resulted in fatal embolism. Femoral phlebitis may result from an extension of the process from the pelvic veins. The embolus arising in the femoral vein is usually dislodged before the phlebitis becomes recognizable clinically. Small emboli which cause pulmonary infarcts (usually 71 per cent) seem to come from the pelvic veins. Obese patients more than 60 years of age seem more susceptible to pulmonary embolism than others.

Mathe<sup>65</sup> stated that distention of the bladder or urethra with air or oxygen for any purpose may prove harmful if not disastrous, if the air or oxygen should enter the venous circulation. Increased intravesical and intra-urethral pressure is more likely to occur in cases of prostatic hypertrophy or in cases of stricture as it prevents the escape of air between the walls of the urethra and the indwelling catheter or cystoscope.

64 Thomas H M, and Alyea Edwin. Pulmonary Embolism Following Urological Surgery. *South M J* 22:737, 1929.

65 Mathe C P. Fatal Embolus Due to Inflation of Bladder with Air. *Stet. Gynec. Obst.* 48:429, 1929.



Mathe considers that the most effective treatment of air embolus is the immediate release of pressure of air in the bladder, artificial respiration and injection of a solution of 2 cc of 1:1000 epinephrine directly into the right side of the heart. Death is due to the arrest of the pulmonary circulation, to gaseous distention of the right side of the heart, preventing function of the tricuspid and pulmonary valves, to too little blood reaching the left ventricle and producing anemia of the vital centers of the brain and to stasis of the coronary vessels. The use of sterile water or mild antiseptic solutions should be substituted for air in inflating the bladder and urethra for diagnostic therapeutic and operative procedures.

## RECURRENT AND SO-CALLED METASTATIC GIANT CELL TUMOR\*

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As information advances, it is obvious that clinical entities are established on the basis of a specific etiology, rather than on abstract classification. For this reason, as additional facts are disclosed, the time honored controversy concerning the inflammatory or neoplastic nature of giant cell tumors and bone cysts is giving place to a discussion of the actual causative processes of these lesions. The evidence presented in a previous paper<sup>1</sup> favored the view that these growths constitute a single entity, and that the giant cell tumor arises as an abnormal phase in the resorption of temporary bone in response to trauma, while the bone cyst presents the healing phase of the same lesion. Nevertheless, in view of the amount of attention recently directed to so-called metastatic giant cell tumors in the literature, it is necessary to present further evidence concerning a certain group of these lesions to delineate them more sharply from the bone sarcomas.

The high percentage of clinical recurrences after treatment in typical giant cell tumor speaks for the progressive nature of this disease. Among 222 cases of giant cell tumor in the surgical pathological laboratory of the Johns Hopkins Hospital there were thirty-one recurrent cases following a primary curettement, and many of these showed repeated recurrences despite surgical intervention. In three additional cases in the series, metastases to the lungs were supposedly responsible for the death of the patient.

An analysis for the reasons for such recurrences has been repeatedly made on the basis of the microscopic picture. In the literature various claims have been set forth by some who believe to see in the microscopic structure of the tumor the explanation of a more persistent and

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1 Geschickter C F and Copeland M M. Osteoclast Fibrosis and Giant Cell Tumor. Arch Surg 19 169 (Aug) 1929

TABLE 1—Cases with Clinical Features Leading to Recurrence

P N No.	Race, Sex and Age	Location	Dura tion, Mo.	Symptoms	Roentgenogram	Treatment	Microscopic 2d oper typical*	Cause of Recurrence	Result
39134	W F 10	Tibia, upper	10	Pain, tumor	Bone shell intact	1st curetting, 1927 2d curetting, 1927	1st oper typical	Shell destroyed	Recurred twice
38912	W F 36	Radius, lower	2	Pain, tumor	Shell de- stroyed	1st curetting, 1925 postoperative radiation cautery, resected, April, 1928	1st oper typical	Age over 30	Living 3 years
38107	W M 10	Femur, lower	24	Trauma, pain, tumor		1st curetting, 1913 2d curetting, Dec, 1925	1st oper typical 2d oper typical	Shell destroyed	Living 1 year
37708	W F 31	Radius, lower	12	Trauma, pain	Bone shell destroyed	1st curetting, June 1926 resection, Sept, 1927	1st oper typical 2d oper fibrous variant	Age over 30 Shell destroyed	Well 2 years
36182	W F 8	Ulna, lower	6	Tumor	Bone shell destroyed	1st resection, May, 1924 radiation Sept, 1924 cauterization, Jan, 1925	1st oper typical 2d oper fibrous variant	Bone shell destroyed	Well 2 years
32901	W F 23	Ulna, lower	36	Loose teeth, tumor	Bone shell perforated	1st curetting, April, 1920 2d curetting, April, 1923 with cauterization	2d oper fibrous variant	Bone shell perforated	Living 3 years
32028	W F 18	Radius, lower	36	Trauma, pain, tumor	Bone shell perforated	1st resection, May, 1921 2d resection, Jan, 1923	Bone healing Few giant cells	Bone shell perforated	Well 5 years
29423	W F 16	Femur, lower	24	Trauma, pain, tumor		1st curetting, Feb, 1917 2d curetting, Oct, 1917 3d curetting, July, 1919 with radium	1st oper typical	Poor curetting (?)	Well 9 years
29306	W F 19	Radius, lower	12	Tumor	Bone shell perforated	1st curetting, March, 1913 resection, June, 1914	2d oper fibrous variant	Bone shell perforated	Well 14 years
28533	W M 25	Humerus, upper	2	Weakness, trauma, pain	Bone shell perforated	1st curetting, July, 1921 radium implanted resection, Jan, 1921	1st oper typical	Bone shell perforated	Well 7 years
27161	W M 50	Humerus, lower	48	Trauma, tumor	Bone shell perforated	1st curetting, Nov, 1919 postoperative radiation 2d curetting, Feb, 1921 with cautery and radium	1st oper typical, foam cells present	Bone shell perforated	Well 7 years
27289	W M 35	Femur, lower	30	Trauma, pain tumor	Bone shell intact	Aspirated, April, 1919 1st curetting, May, 1919 with cautery 2d curetting, June 1919 with cautery	Fibrous variant second and third operation	Treated as osteomyelitis	Well 8 years



malignant course More recently Goforth<sup>2</sup> has attempted to grade the microscopic picture to show the gradual transition of benign giant cell tumor to osteogenic sarcoma

Microscopic studies of giant cell tumors in this laboratory have been carried out in an effort to confirm or possibly to elucidate the alleged malignant transformation of giant cell tumors If it is true that these tumors may show a gradual transition to osteogenic sarcoma and kill by metastases, and reasons for this transition may be developed, then we have established a most valuable approach to the nature of a malignant condition so far as it applies to bone The present conception of the giant cell tumor as a benign growth would have to be somewhat altered so far as this lesion would then present the characteristics of a pre-sarcomatous growth However logical the existence of such histologic gradations toward a malignant condition may appear, a survey of the data from many different sources, it will be shown, does not support such contentions

In approaching this problem microscopic analysis alone is insufficient, and much is to be gained from a study of the physiopathologic processes underlying both effective and unsuccessful methods of treatment For this reason the study of recurrent and metastatic giant cell tumors presented here includes a survey of all the factors related to this group of tumors including both clinical and embryologic features

For purposes of analysis it has been found convenient to group the lesions under discussion into four groups The first comprises microscopically benign giant cell tumors with clinical features leading to recurrence The second group includes giant cell tumors which resemble sarcoma microscopically, with or without clinical recurrence In the third group are placed those giant cell tumors which are associated clinically with metastases and death The fourth group is composed of osteogenic sarcoma containing giant cells and resembling microscopically giant cell tumor A discussion of these four groups is followed by an analysis of the clinical results following various types of treatment in over 200 giant cell tumors

#### I BENIGN GIANT CELL TUMOR WITH CLINICAL FEATURES LEADING TO RECURRENCE

In this group of lesions the original tumor was always characterized by a microscopic structure typical of the usual benign giant cell tumor The failure of these lesions therefore to heal after a primary curetting cannot be explained on a histologic basis A study of the twenty-six cases in this group, however (table 1), reveals that the cause of the recurrences is to be ascribed either to a poor selection in choosing the type of treatment for the individual case or to an incomplete operation

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<sup>2</sup> Goforth, J L Giant Cell Tumor of Bone, Arch Surg **13** 846 (Dec) 1926

Either the operator elected to curet a lesion that was too far advanced or at a disadvantageous age and site, or in performing the curettement, there was incomplete removal of the tumor and usually failure to follow with chemical or thermal cauterization

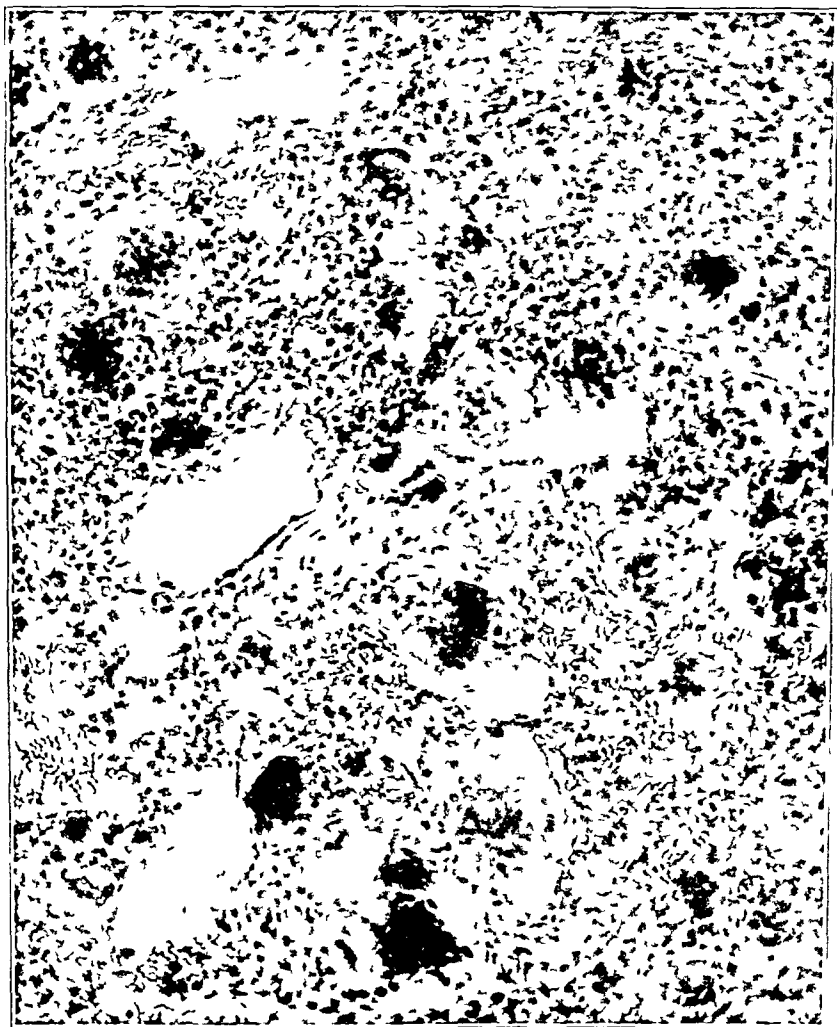


Fig 1 (P N 27291 metastatic case 2) —Structure of a giant cell tumor that recurred four times. The photomicrograph shows the original lesion at the time of primary curettement, which resembles the typical giant cell tumor. Section for the photomicrograph was secured through the courtesy of Dr B C Crowell from the Bone Registry of the American College of Surgeons.

*Microscopic Analysis*—While some authors<sup>2</sup> claim to be able to distinguish in the section of the original giant cell tumor, the cause for

its subsequent recurrence, the lesions in the present group show no peculiarities in the microscopic picture which would bear out such a claim. Tissue taken from the original lesions in the twenty-six cases already referred to shows a predominance of large multinucleated giant cells, which average over 30 to the low-power field and contain

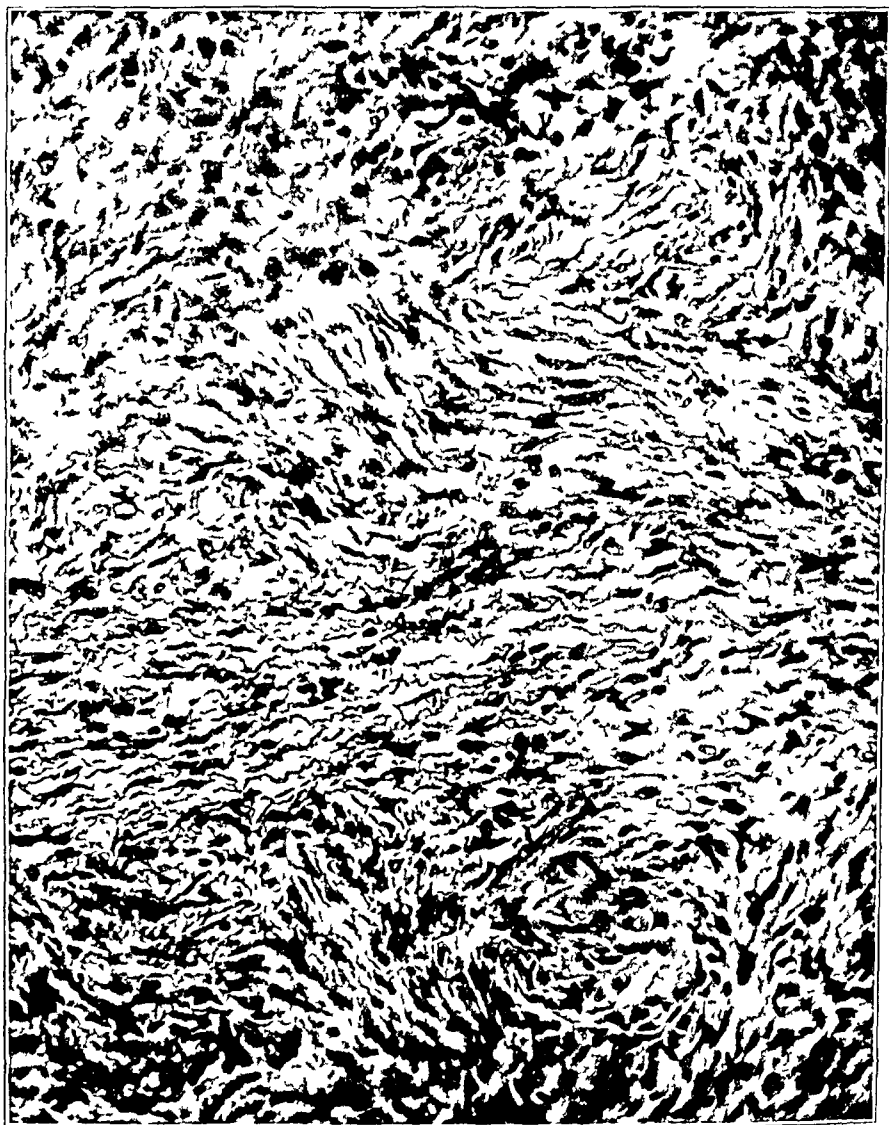


Fig 2 (P N 27291, metastatic case 2) —Photomicrograph of the same tumor shown in figure 1, after the fourth operation. The unusual amount of fibrous proliferation is due to a healing reaction, but was incorrectly diagnosed sarcoma by many competent pathologists. The healing reaction has been accentuated by roentgen and radium therapy.

from 15 to 200 nuclei per cell (fig 1). These giant cells are embedded in the round cell stroma typical of all benign giant cell tumors, and in the sections taken from the second operation after the tumor has recurred,

there is no histologic change toward osteogenic sarcoma or what may be called a malignant giant cell variant. Unless the lesion has become infected, the histologic change following recurrence is usually characterized by an increase of fibrous tissue (fig 2). Numerous spindle cells and fibroblasts are found among the round cells indicating nature's attempt at a healing reaction. Occasionally, foam cells are found in the sections, and although this entitles the lesions to the name of xanthoma variants, there is no significant change in the typical microscopic struc-

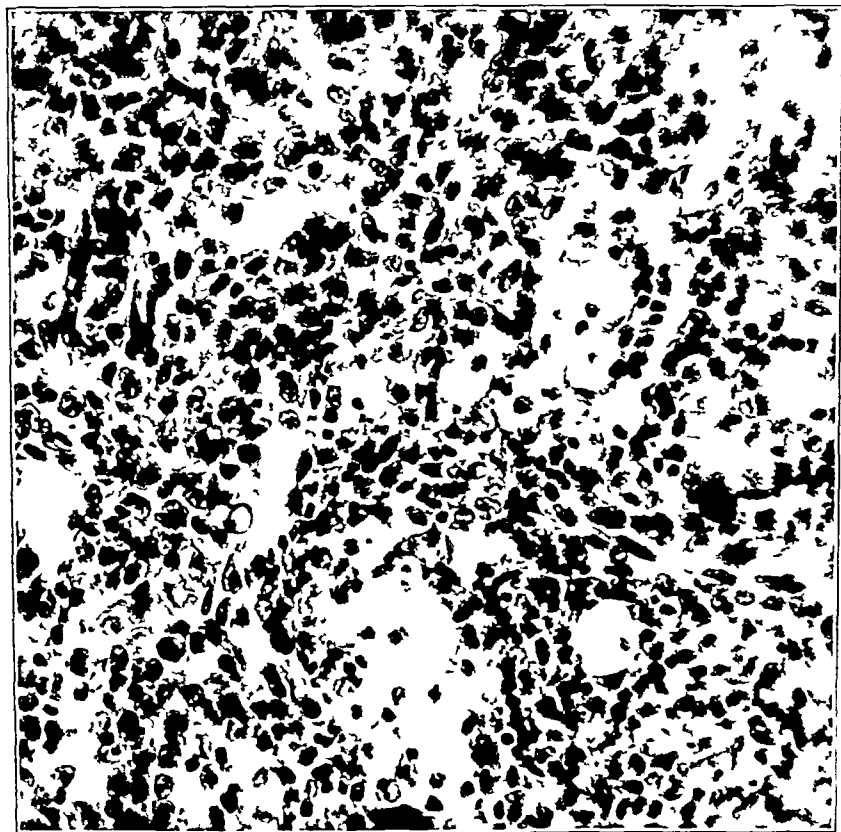


Fig 3 (P N 27461)—Foam cells in a typical giant cell tumor that recurred. These so-called xanthoma cells are the result of extension by the tumor into the soft parts.

tures (fig 3). It is important to emphasize here as well as elsewhere, that we believe that such foam cells are associated with perforation of the bony capsule and extension of the tumor into neighboring soft parts which furnish the lipoids characteristic of these xanthoma cells.

Since the microscope is of no aid in disclosing the reasons for recurrence in this group of tumors, it is necessary to look into the clinical features of the growth and the methods of treatment in order to explain



the failure of these tumors to follow the usual course and heal after a primary curettement

*Clinical Features Leading to Recurrence*—A review of the clinical features of this group shows that age must be considered as a contributory factor to recurrence. In order to determine the importance of this factor, 105 cases in which the patients were submitted to primary curettement were selected, and the ages of those in whom curettement

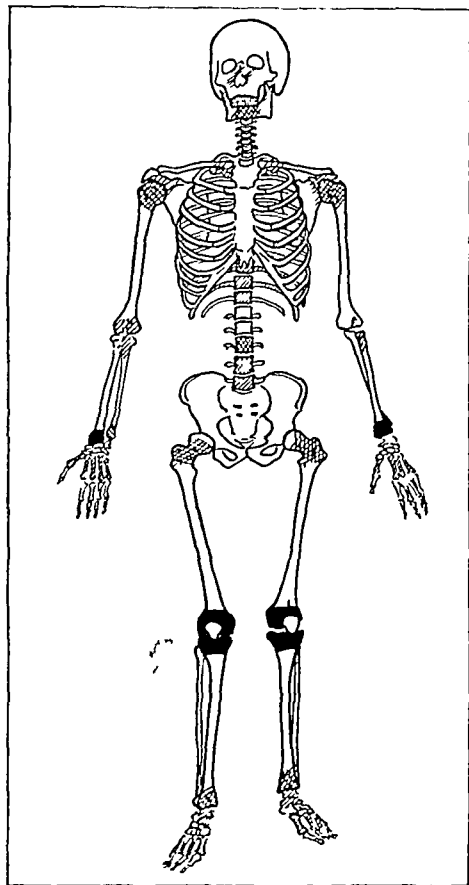


Figure 4

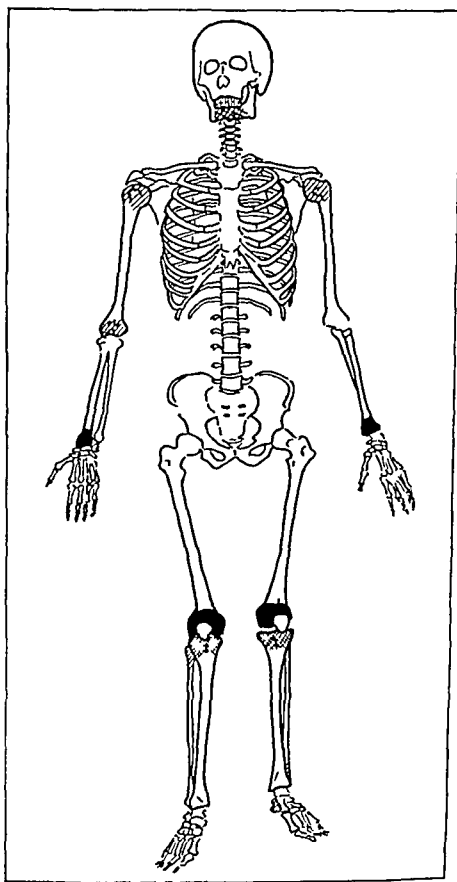


Figure 5

Fig 4—Chart showing the skeletal sites involved by 222 giant cell tumors. The solid black area indicates the most frequent sites, the checked areas, the common sites, and the diagonal lines, the occasional sites. Other sites are exceedingly rare. Note that the epiphyseal regions are most often affected.

Fig 5—Chart showing the skeletal sites involved by thirty-one recurrent giant cell tumors. The solid black area indicates the most frequent sites, the checked areas the common sites, and the diagonal lines the occasional sites (compare with fig 4).

was successfully done were compared with the ages of those who suffered recurrence. In the group of patients with giant cell tumors cured by curetting, 21 per cent were over 30, and 41 per cent were under 21. In the recurrent groups of giant cell tumor, 42 per cent were over 30 years

of age and only 16 per cent were under 21. There is, therefore, a contrast between the ages in the recurrent and in the nonrecurrent groups with a definite tendency for the giant cell tumor to recur more readily in persons more than 21 and even more frequently in those more than 30 years of age. This is to be explained by the fact that cortical bone declines in its power to heal and ossify after the age of 21, and as we have pointed out previously, this cortical bone is a primary factor in the healing reaction about a giant cell tumor.

The location of the tumor is also of some significance in regard to recurrence. While recurrent giant cell tumors occur in most of the sites where giant cell tumors arise, the lower end of the radius appears to be a favorite location for the return of the lesion after curetting (figs 4



Fig 6 (P N 37708) —Roentgenogram of a giant cell tumor of the lower part of the radius showing extensive destruction of the bone shell which led to a recurrence of the tumor after curetting

and 5). The ordinary giant cell tumor affects most frequently the upper part of the tibia, and the lower part of the femur and of the radius. The upper part of the tibia shows relatively few recurrences (8 per cent) and the lower part of the femur a moderate number (39 per cent), while in a series of sixteen curettings in the lower part of the radius, 50 per cent recurred. The explanation of these frequent recurrences in the radius lies in the destruction of the bone shell, which usually has progressed to a further degree in this nonweight-bearing bone than in the bones of the leg before the patient is aware of severe symptoms in the use of the limb. The average duration of symptoms is twenty months in the radius compared with fourteen months for the usual giant cell tumor (fig 6).

Both age and the site of recurrences emphasize the influence of cortical bone in the healing of giant cell tumor after curettement.

Primarily, the most valuable asset in the cure of a giant cell tumor is the preserved shell of cortical bone with an intact and competent vascular supply. This is evidenced by the spontaneous healing of giant cell tumors to produce a bone cyst in the metaphysis and shaft of the long bones in which there is a substantial layer of cortical bone with a richly vascularized subperiosteal mantle. The origin of the abnormal growth is dependent on the temporary dysfunction of this portion of the bone following a trauma.

Roentgenograms and gross specimens emphasize that the giant cell tumor most frequently recurs because curettement rather than resection has been undertaken in a tumor that has destroyed too much of the bone shell before the time of surgical intervention (figs 7 and 8). The



Fig 7 (P N 32924) —Roentgenogram of a giant cell tumor in the lower end of the fibula, similar to the case shown in figure 6. Advanced destruction of the shell of cortical bone was responsible in all probability for the recurrence after curettement in this case.

perforation of a giant cell tumor into the soft parts is more to be feared because of the cortical destruction antecedent to the perforation than because of infiltration and the danger of incompletely removing the soft part tumor (table 1).

Treatment so far as it involves the selection of the type of operation in any particular case and also the skill with which such therapy is applied constitutes the major cause for recurrences. Obviously, curettement in a patient over 35 years of age with a giant cell tumor in the lower end of the radius that has destroyed the major part of the bone shell invites recurrence. Resection with subsequent transplantation of bone is to be preferred. In this way the selection of the mode of treatment determines the clinical result. In an equal number of cases the

failure to use chemical or thermal cauterization after curettement predisposes to recurrence. In seven of the cases in this series the recurrence of the tumor could be ascribed to partial curettement. Usually the failure to remove all of the tumor was due to an erroneous diagnosis which led to simple aspirations or to incomplete excision, in the belief that a suppurative condition existed. In one case the operation was incomplete because undue hemorrhage was encountered.



Fig 8 (P N 32924) —Gross specimen of the tumor shown in figure 7. The shell is perforated and infection followed (fig 11).

In curetting care should be taken to remove as much of the cancellous bone involved as possible, and at the same time to preserve a maximum amount of the cortical bone shell with intact blood supply. When the surgeon is over liberal in the removal of cortical bone, repeated operation is often necessary and each time more and more of the cortical bone is sacrificed, until cure by curettement becomes impossible.

The fact that no giant cell tumor has recurred after primary radical resection or amputation emphasizes the fact that the mode of treatment and not the histology of the tumor is the primary factor in recurrence.

As Bloodgood<sup>4</sup> has repeatedly pointed out, the typical giant cell tumor is benign, and conservative treatment by efficient curettement and cauterization is the operation of choice in most instances. This is particularly true when resection because of the bone involved would be equivalent to amputation. But in elderly patients and in cases in which much of the bone shell is destroyed and in sites such as the fibula, radius and humerus when resection with transplant of bone will restore function, discrimination between curettement and resection should be carefully made, and the possibilities of preliminary treatment by roentgen therapy seriously considered. Because of the close relationship of these lesions to the usual bone cyst, the possible benefits resulting from collapsing the cavity remaining by crushing<sup>5</sup> or by filling with bone chips, must also be weighed.

## II MALIGNANT VARIANTS AND DIFFERENTIAL MICROSCOPIC DIAGNOSIS IN GIANT CELL TUMOR

In the cases considered in this group, seven lesions are grouped together which showed under the microscope characteristics resembling osteogenic sarcoma (tables 2 and 3). Practically all of these cases were submitted to various pathologists for diagnosis, and in most instances there was a striking lack of agreement among those most competent to judge. Although ultimate clinical results favor the conclusion that the tumors were benign (no deaths are recorded in the follow-ups), still in three instances (P N 29327, P N 39404, P N 26792) the microscopic structure is indistinguishable from certain varieties of osteogenic sarcoma.

This small group of cases selected from among 222 cases of giant cell tumors of bone demonstrates practically all the points of confusion arising in the differential microscopic diagnosis of giant cell tumor. All the important variations in the histologic picture of this tumor are depicted, such as changes due to necrosis from poor fixation, alterations dependent on recurrence and infection, modifications due to partial healing with fibrosis, changes brought about by irradiation or by infiltration of adjacent tissues, as well as the actual presence of osteogenic sarcoma in the sections. An analysis, therefore, of this small group of so-called malignant variants of giant cell tumor serves admirably as a study in the differential diagnosis of this growth, as far as microscopic changes are concerned. It serves to emphasize the importance in microscopic diagnosis of a familiarity on the part of the pathologist with changes produced in the histology of giant cell tumor by previous operations.

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4 Bloodgood, J. C. The Conservative Treatment of Giant Cell Sarcoma, *Ann Surg* 56 210, 1912

5 Henderson, M. S. Giant Cell Tumor of the Upper End of the Femur *Minnesota Med* 11 542 1928

TABLE 2—*Malignant Variants of Giant Cell Tumor with Recurrence*

P. N.	Race and Age	Sex	Location	Duration, Mo.	Symptoms	Roentgenogram	Treatment	Microscopic	Cause of Microscopic Change	Result
6170	W	12	Lower jaw	12	Tumor	Bone shell intact	Partial curetting, 1923 by dentist 2d curetting, Oct., 1921	2d oper. young fibrous tissue with new bone	Healing after 1st operation	Well 3 years
6021	W	M	Ilium, lower	3	Trauma, pain, tumor	Bone shell perforated	1st curetting, April, 1923; 2d curetting, May, 1923 with cauterization resection, Aug., 1923	1st oper. necrotic tissue* 2d oper. infected tissue 3d oper. infected tissue	Necrosis and infection	Well 5 years
6077	W	M	Emur, lower	1	Trauma tumor	Bone shell intact	Exploration, Oct., 1920 followed by infection 1st curetting, Nov., 1921 with cauterization amputation, 1922	2d oper. infected tissue 3d oper. malignant variant Section indistinguishable from osteogenic sarcoma	Infection	Well 6 years
6092	W	M	Humerus upper	21	Trauma, pain, tumor	Bone shell intact	Partial curetting, 1916 2d curetting, July, 1916 3d curetting, July, 1920	2d oper. infectious changes	Infection	Well 8 years
6012	C	M	Vertebrae	18	Pain, tumor		Partial excision, 1919 Further excision, 1919 Further excision, 1920	3d oper. infectious changes	Infection	No follow up

\* In this table malignant variant refers to microscopic changes dependent on recurrence in every instance but this

irradiation, partial healing, infection, invasion of soft parts and poor fixation, in comparison with the typical structure of both giant cell tumor and osteogenic sarcoma

*Clinical Features*—The clinical features of these "malignant" variants are given in tabular form in tables 2 and 3. It will be seen that five of seven cases recurred after initial treatment of curetting or excision, and that the microscopic variations are generally associated with a second or third operation with intervening infection. In other words, instead of the so-called malignant microscopic structure being the cause of the recurrence, the reverse is true—the infection of the recurrent tumor is usually the cause for the microscopic change. Death has not been recorded in any of the seven cases, but in table 2, two patients alive, five and six years after treatment, respectively, were subjected to resection or amputation, and such treatment which may result in cure

TABLE 3—*Malignant Variants of Giant Cell Tumor Without Recurrence or Metastasis*

P N	Race, Sex and Age		Location	Duration Mo	Symptoms	Roentgeno gram	Treatment	Microscopic	Result
39184*	W	F 15	Scapula, neck	6	Pain, tumor	Shell intact	Curetted July, 1927	Calcified cartilage in the malignant variant	Well 1 yr
26792*	W	M 16	Humerus, upper	16	Trauma, pain	Shell thin perforated	Curetted, Oct, 1920, with cautery radium and toxins	Calcified cartilage in the malignant variant	Well 8 yr

\* See P N 35226 and P N 40872, included with metastatic giant cell tumors and microscopically identical with these two cases

in genuine sarcoma must be considered in evaluating the character and clinical course of the growth. In table 3, both patients for whom data are given are in the sarcoma age. The tumor did not recur after curetting in either case, but the resemblance to a form of osteogenic sarcoma observed in the original tumors is sufficient to make the diagnosis of giant cell tumor exceedingly doubtful.

*Microscopic Analysis*—In the cases listed in table 2 all of the lesions recurred, and unfortunately verified sections from the original tumors were obtained in only one instance. The condition in all five cases was diagnosed osteogenic sarcoma by the majority of the pathologists passing on the sections. In the case in which sections from the first operation were seen (P N 32924), poor fixation resulting in necrosis was responsible for the inability to distinguish between sarcoma and a variant of giant cell tumor (fig 9). In the other four cases, owing to lack of knowledge of the history or to actual errors in the clinical or clerical records the pathologist making the diagnosis was not informed that he was looking at a recurrent lesion and not the original tumor. In one

case (P N 36170) a marked healing reaction resembled fibrosarcoma, and in the other three cases (table 2) infection accounted for the marked pyknosis and cloudy swelling of the nuclei mistaken as a feature of osteogenic sarcoma. Unfamiliarity with the changes in giant cell tumor produced by partial healing after a primary operation or by infection was therefore the cause for most of the diagnostic errors in this group.

In the case in which marked healing reaction occurred (fig 2), a careful study of the sections under a high power lens showed that the



Fig 9 (P N 26091)—Photomicrograph of a poorly fixed specimen of giant cell tumor. Necrosis similar to this led to an erroneous diagnosis of sarcoma in case P N 32924.

young proliferating cells were early fibroblasts participating in a reaction referred to by us as fibro-ostosis.<sup>1</sup> In the cases in which the patients were previously infected the pyknosis and cloudy swelling resulting simulated malignancy particularly when examination was made under high magnification (fig 4 and fig 11 ARCH SURG vol 19 pp 172 and 202 respectively). The pyknosis resembled early mitosis so often seen in sarcoma and the swollen nuclei undergoing degeneration resembled the large pale nuclei seen in a malignant condition of the bone. The



low magnification is perhaps more reliable in arriving at a trustworthy conclusion. When thus examined there was more loose fibrous tissue, a less cellular stroma and more nuclear debris than is seen in sarcoma under lower magnification. The giant cells present in these malignant variants were larger and more numerous and contained over 15 nuclei to the cell, which is not typical of osteogenic sarcoma. Analysis under high power magnification of the large vesicular nuclei in these infected cases showed that often they were composed of several smaller nuclei which were undergoing clumping and losing the finer markings of their former structure, with the gradual formation of an amorphous mass.

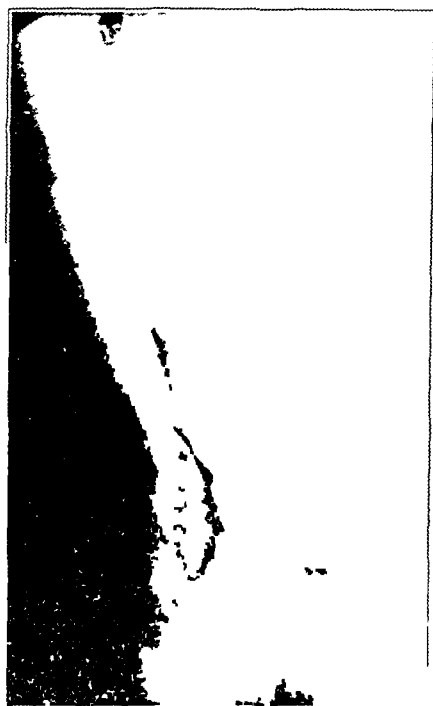


Fig 10 (P N 32924) —The granulating wound of the tumor shown in figures 7 and 8

In any case, therefore, in which a bone tumor containing frequent large giant cells averaging over 15 nuclei per cell is seen with evidence of round cell and polymorphonuclear infiltration and frequent areas of hemorrhage surrounded by young loose fibrous tissue, the pathologist should be on his guard against making a diagnosis of sarcoma and wary lest the apparent malignancy of the nuclear material is in reality pyknosis and cloudy swelling dependent on infection and degeneration (Bloodgood<sup>6</sup>).

In table 2 there is one exception to this rule (P N 29327). The tumor in the lower part of the femur of a white man, aged 19, was

6 Bloodgood, J. C. Why Do Giant Cell Tumors Recur? To be published

explored after symptoms of four months' duration following trauma. The original diagnosis was giant cell tumor, but microscopic examination was not made, and the wound was allowed to become infected. Sections from a curetting performed a year later (fig 12 *A*) showed the malignant variant due to infection, but sections from a subsequent recurrence which led to amputation one year later showed unquestionable osteogenic sarcoma (fig 12 *B*). The patient is alive and well six years

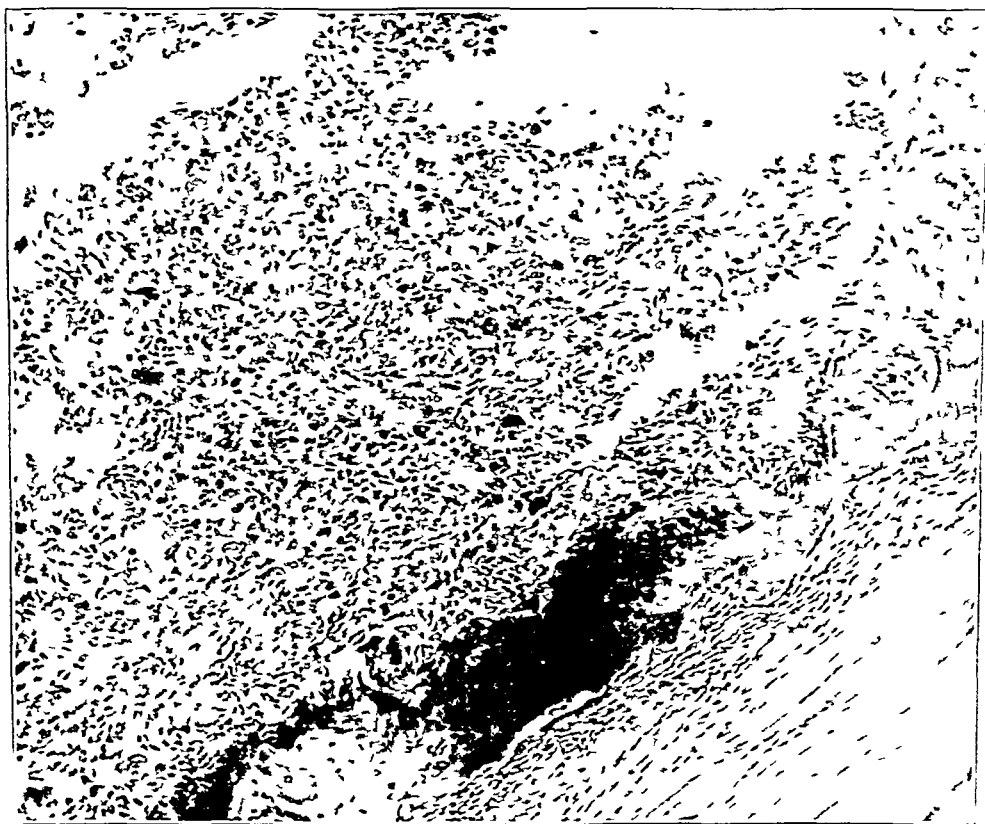


Fig 11 (P N 32924) —Low power photomicrograph of the tumor shown in figures 7, 8 and 10. Infection has occurred resulting in the so-called malignant variant. Pyknosis and cloudy swelling of the nuclei resemble the cells seen in osteogenic sarcoma.

after amputation, but this must be looked on in all probability as an amputation cure in sarcoma. When this case is compared with those in Section III of this paper, it warrants consideration as a case of sarcomatous transformation in a giant cell tumor. But the sections of the original exploration are not available and those from the second observation are atypical and cannot be proved to be benign, whereas the failure of the lesion to heal after infection might well have stimulated

a second neoplastic process of sarcomatous nature. The matter will be discussed further under the metastatic group of giant cell tumors. This case was included in table 2 because the patient is living and is without signs of metastases.

Although the age of the patients, the clinical course and the microscopic structure of the tumors in the two cases listed in table 3 are typical of a chondroblastic form of osteogenic sarcoma, giant cells are present

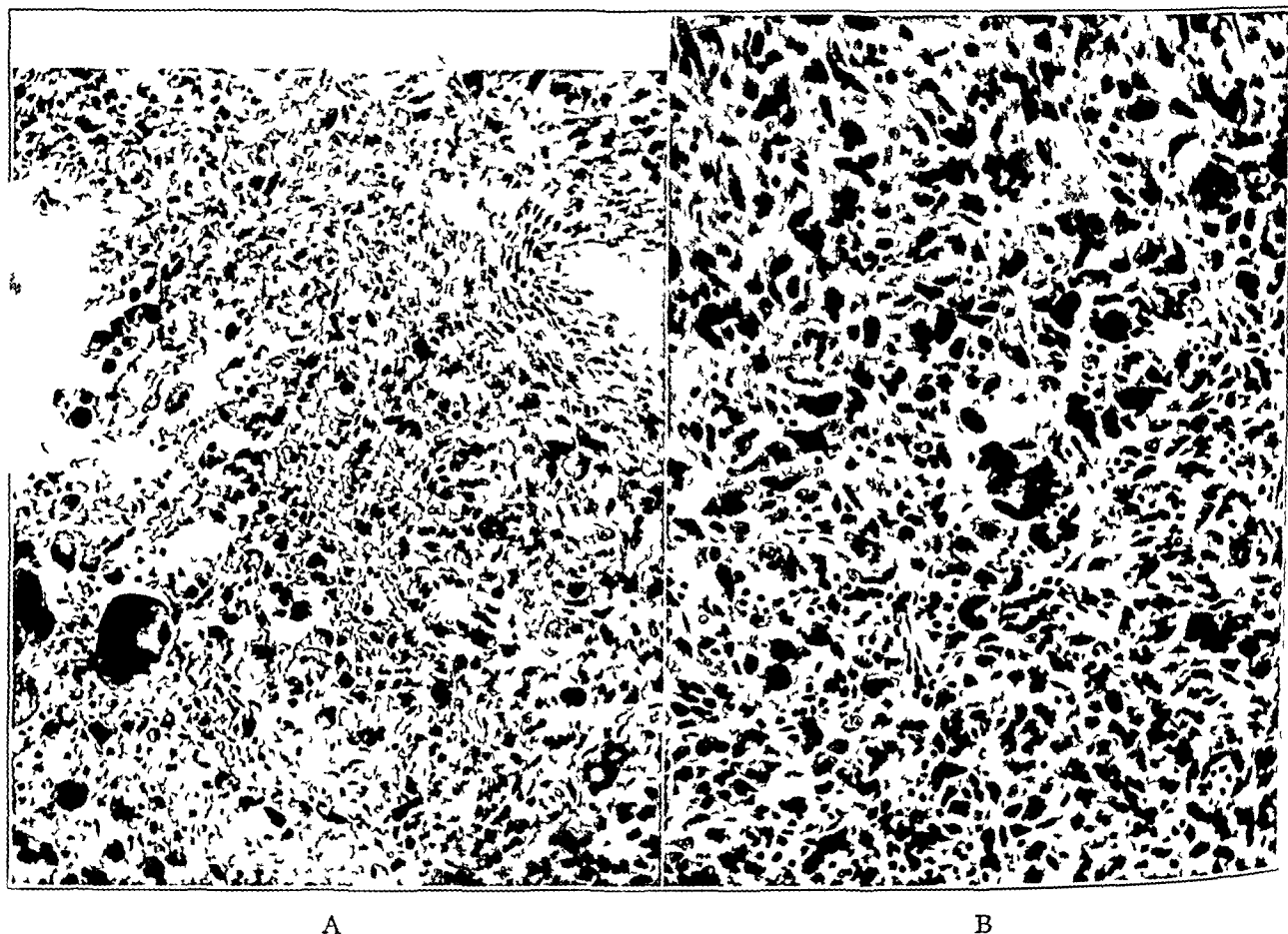


Fig 12 (P N 29327) —*A* Photomicrograph from the second operation on an alleged malignant variant of giant cell tumor. Infection has occurred, and early osteogenic sarcoma is simulated by the large swollen nuclei. Note the unusual amount of nuclear debris. *B* Photomicrograph from the third operation on the same tumor as shown in *A*. This section is indistinguishable from osteogenic sarcoma.

in the sections, and both patients are alive after curetting, without signs of recurrence. In one case (P N 39484) only one year has elapsed since operation, and the ultimate result may confirm this as sarcoma, but in the other case with similar microscopic structure, the patient (P N 26792)

is living eight and a half years after curetting followed by deep roentgen and radium implantation, in addition to erysipelas and prodigious toxins (Coley)

In this last case (figs 13, 14 and 15) which is the well known case of Dr. Bunts of Cleveland, the patient had a lesion in the upper part of the humerus which was originally diagnosed sarcoma by most of the pathologists who saw the sections, with a minority dissenting in favor of giant cell tumor. Despite the fact that the survival of the patient has swung the pendulum of opinion to a diagnosis of "malignant variant" of giant cell tumor a study of over thirty cases of similar microscopic structure shows the lesion to be a malignant grade of osteogenic sarcoma. The cure must be ascribed to the radium and roentgen treatments.



Fig 13 (P N 26792)—Roentgenograms of a lesion originally diagnosed sarcoma and then giant cell tumor of the so-called malignant variant type which must now be classed as a form of chondroblastic sarcoma. Note the periosteal lifting at the lower margins of the tumor and the fuzzy periosteal reaction. There is no maximal area of bone destruction immediately beneath the cortex as in giant cell tumor. The roentgenogram on the right shows radium implantation in the tumor.

The form of "malignant variants" shown in table 3, therefore, we believe subject to reinterpretation. Under the microscope these tumors show a rapidly proliferating and early form of cartilage cell which produces only an abortive form of chondromatrix transformed here and there by calcification (fig 14). The giant cell areas invading the tumor represent it would seem an attempt on the part of the normal bone structures to vascularize and resorb this malignant tissue by a process typical of the resorption of normal calcifying cartilage in the human embryo.<sup>1</sup> This point will be brought out again in this paper in discussing metastatic giant cell tumors. Since it is so at this point that in

making a microscopic diagnosis of giant cell tumor the pathologist must be on his guard, not only against labeling benign infected giant cell tumors sarcoma, but also against calling this type of sarcoma showing giant cell areas, a benign tumor.

For the purpose of completing a differential diagnosis we shall revert briefly to the question of xanthoma variants of the giant cell tumor, since certain authors consider these among the malignant variants of giant cell tumor (fig 3). The view taken here is that the foam cells

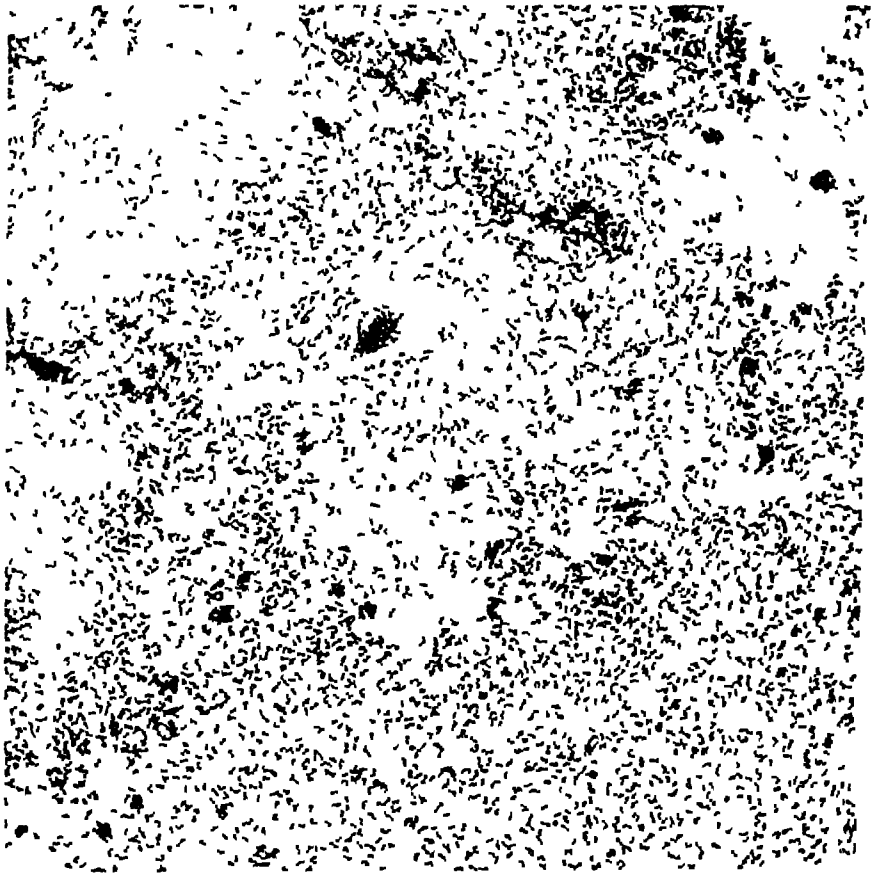


Fig 14 (P N 26792) —Low power photomicrograph of the tumor shown in figure 13. Note that in addition to the giant cells, there is a cartilaginous matrix undergoing calcification in the upper portion of the picture which is better seen in figure 15.

are the result of a perforation of the bone shell, and in themselves indicate nothing more than that the tumor has reached the soft parts. They signify nothing in regard to the anaplastic tendencies of the tumor and are independent of its essential components.

In summarizing this study of the "malignant variants" of giant cell tumor, two questions of long standing may be answered. First, what is the relation of the microscopic picture of a "malignant variant" to recur-

ience after curetting and second what is the relation of the "malignant variant" of giant cell tumor to osteogenic sarcoma

In answer to the first, it may be said that 'malignant' modification in the microscopic structure of a giant cell tumor is usually the result and not the cause of recurrence. When the 'malignant variant' structure is primary and recurrence results, metastasis is apt to follow, showing that in a few instances a genuine sarcoma has been masquerading under the false diagnosis of giant cell tumor

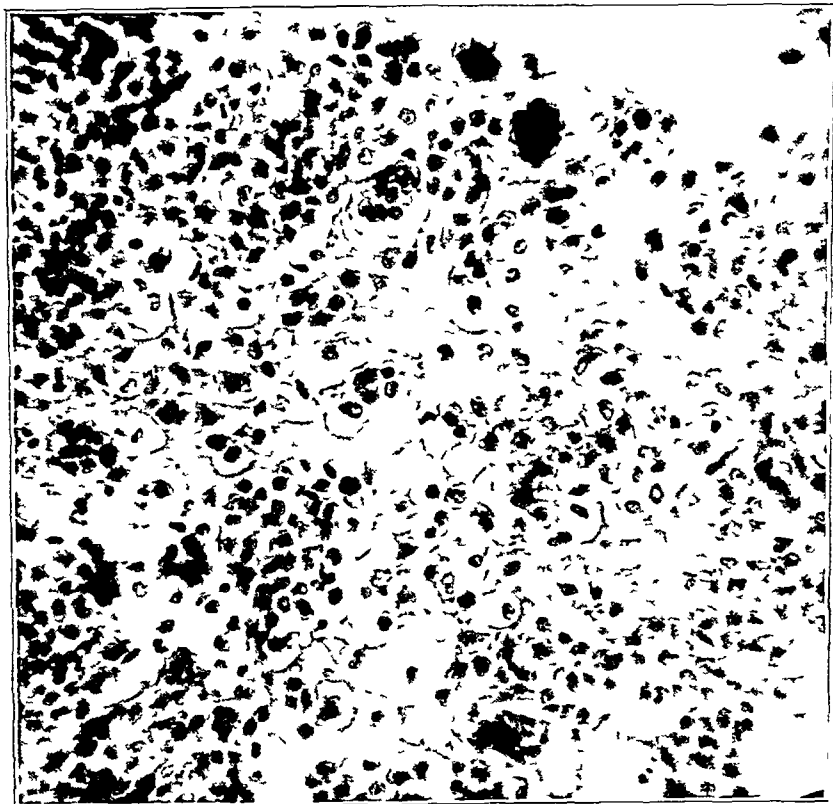


Fig 15 (P N 26792) —High power photomicrograph of the cartilaginous area shown in figure 14. This type of cartilaginous matrix has never been observed in any of the benign giant cell tumors in our series of over 200 cases.

And on this score, in answer to the second question, of the relation of such sarcomas to giant cell tumors we may say that the giant cell phase of osteogenic sarcoma is usually a secondary process in which giant cells are invading malignant areas of chondroblastic sarcoma in response to the abortive calcified cartilage present. Here the cartilaginous bone is primary and the giant cell areas secondary. In benign giant cell tumor the giant cell areas are primary and are secondarily invaded by bone not of a cartilaginous variety but of fibroblastic origin.

From the point of view, therefore, of differential diagnosis, the question to be decided is the type of new bone formation present. The abortive chondroblastic type signifies sarcoma.

### III THE METASTATIC GROUPS

Recently there has been an attempt to show that the typical giant cell tumor called benign may occasionally metastasize and produce death. Stone and Ewing,<sup>7</sup> Goforth,<sup>2</sup> and Finch and Gleave<sup>8</sup> are among others who have published reports of unusual giant cell tumors, apparently typical in structure, but peculiar in behavior. Goforth stated that "an occasional case is met with, which although locally malignant, and in a few instances actually metastasizing, apparently does belong to the giant cell tumor group." Similar statements are frequently occurring in the literature with illustrative case reports, and it would seem that there is a tendency for the pendulum to swing away from the more fundamental contributions of Nelaton,<sup>9</sup> Paget<sup>10</sup> and Bloodgood<sup>11</sup> on the benign nature of the giant cell tumor.

Since the fountain head for such statements on the admittedly unusual behavior of these tumors is to be found in the cases reported, the determination of their veracity must be made by an analysis of the cases cited. We have gathered eight such cases from the literature and from the records of the surgical pathological laboratory of the Johns Hopkins Hospital. The value of the material thus gathered depends on the facts that we have the actual sections available for study on all of these cases kindly sent to us from various clinics, and that the eight cases analyzed subsequently represent the unusual members of a much larger series from the clinics of New York, Philadelphia, Chicago, Baltimore, Canada and England—in all a series of well over 500 cases.

Two important conclusions stand out in analysis of this material. First, in no case has a nodule of typical giant cell tumor ever been found in the lung, for wherever these metastatic nodules have been examined, they have shown the histology of osteogenic sarcoma (fig 21). Second, in no one case has the association of an originally benign and typical giant cell tumor in the bone with a secondary metastatic osteogenic sarcoma in the lung been proved.

7 Stone, W. S., and Ewing, J. An Unusual Alteration in the Natural History of a Giant Cell Tumor of Bone, *Arch. Surg.* 7: 280 (Sept.) 1923.

8 Finch, E. F., and Gleave, H. H. A Case of Osteoclastoma with Pulmonary Metastasis, *J. Path. & Bact.* 29: 399, 1926.

9 Nelaton, E. *Tumeurs benignes des os*, Paris, 1860.

10 Paget, J. *Surg. Path.*, Philadelphia, Lindsay & Blackiston, 1854, Lecture 27, p. 446.

11 Bloodgood, J. C. Benign Bone Cysts, Osteitis Fibrosa, *Ann. Surg.* 52: 145, 1910.

These are the two fundamental points brought out subsequently. On the whole, pathologists are agreed that regardless of their opinion as to the nature of the original growth the actual metastasizing lesion is not giant cell tumor but an osteogenic sarcoma. It may be taken as proved that a giant cell tumor found to be typical by a competent pathologist is safely treated conservatively. The question, therefore, is not whether a giant cell tumor will metastasize—it never does—but whether these growths when they recur after improper treatment will undergo malignant change and give rise to osteogenic sarcoma. This question has not been settled, but the evidence brought forth subsequently would seem to answer it in the negative.

The eight cases to be considered are reviewed in abstract and divided into three groups. All of the cases were studied in one or more phases, microscopically, by the authors. All were followed clinically and all terminated in death. In group 1 (two cases), careful inquiry into the nature of the death has shown the cause of the fatality to be other than neoplastic, and metastases were erroneously considered to have occurred. In group 2 (four cases) the nature of the primary lesion was never adequately proved. It was, however, evidently benign in each case, and was followed eventually—*after an interval of years*—by a sarcoma with metastases. In group 3 (two cases) the microscopic structure, the brief clinical course and the nature of the death, all point to a primary sarcoma of bone erroneously diagnosed as a benign giant cell tumor.

The key to the analysis in this group of cases is to be found in a proper understanding of the fundamental pathologic processes of both giant cell tumor and osteogenic sarcoma in relation to the embryology of bone. We consider the point well established that giant cell tumor tissue represents an exaggerated normal phase of the resorptive ("osteoclastic") process in the production of bone from cartilage (Geschickter and Copeland<sup>1</sup>). We also will endeavor to show in a subsequent article, based on the study of 400 cases of osteogenic sarcoma that this group of tumors rehearses in its various phases the embryology of normal bone, and therefore there will be present at times the osteoclastic or resorptive stage of temporary bone characterized by the presence of giant cells. It is thus evident why on further analysis supposedly malignant giant cell tumors so often turn out to be merely areas in which a bone-forming sarcoma exhibits a resorptive phase marked by giant cells typical of the histogenesis of normal bone via the cartilaginous route.

The first two cases (1 and 2) in group 1 were both erroneously placed in the metastatic group since on final analysis it was found that the patients died of causes other than tumor.



## REPORT OF CASES

CASE 1 (P N 34402, fig 16, Dr W G Turner and Dr T R Waugh<sup>12</sup>) — *Bone tumor, giant cell, femur, lower end, left, metastatic (?) to femoral vein dead from pulmonary embolism*

*History*—Frank W, a white man, aged 41, patient of Dr Turner and Dr Waugh, was admitted to the Royal Victoria Hospital, Canada, complaining of trauma which had occurred five months previously, after striking the left knee on a piece of stone. Pain and swelling with limp had been present for four months and swelling of the thigh and groin for three weeks. He was admitted to the orthopedic service of the Royal Victoria Hospital on May 31, 1922.

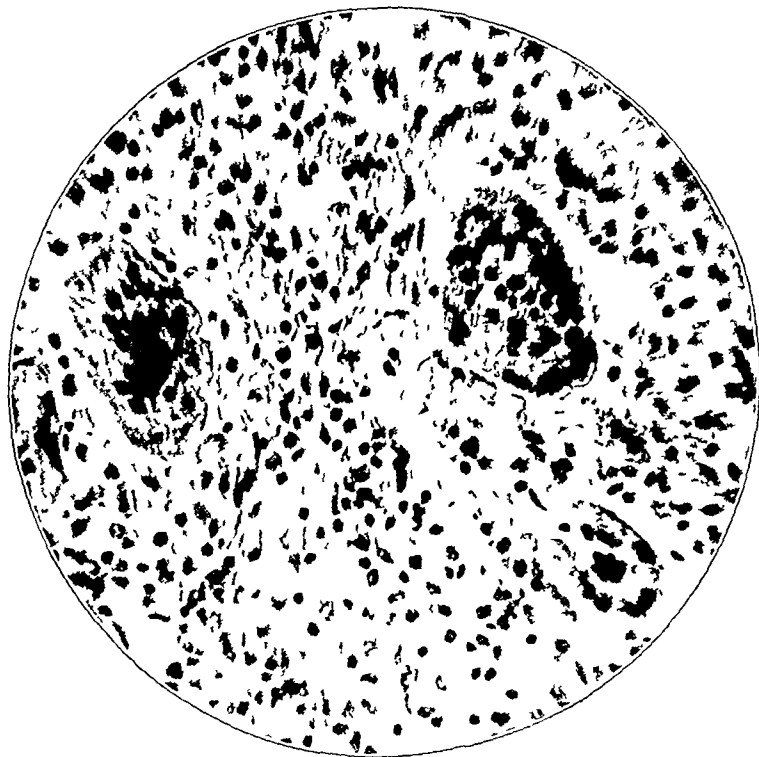


Fig 16 (P N 34402, metastatic case 1 of Dr Turner and Dr Waugh) —Giant cell tumor with spindle cell stroma in a venous thrombus occurring in the wall of the femoral vein at the groin. Photomicrograph reproduced from the article of Dr Turner and Dr Waugh through the courtesy of the authors.

*Examination and Course*—The entire left leg was hard, edematous and swollen. Roentgen examination showed perforation of the bone shell, partial destruction of the epiphysis and a tumor encapsulated by periosteum. The lungs were clear.

Roentgen treatment was begun in March, 1922, and continued for six weeks. On June 8, 1922, the leg was amputated at the hip joint. Microscopic examination made by Dr Bloodgood revealed giant cell tumor with spindle cell stroma in a thrombus. The patient died six months after injury. On July 8, 1922, pulmonary embolism was found at necropsy, but no metastases of the lung were found.

<sup>12</sup> Turner W G and Waugh, T R. *Am Surg* 78:846 (Dec) 1923.

*Comment*—Venous and pulmonary involvement and death were embolic in nature and not metastatic, to be ascribed to accidental causes and not to the malignant condition of the tumor. In all probability the duration of symptoms was longer than was recalled by the patient.

CASE 2 (P. N. 27291, figs 1 and 2, JCB No 10290, Dr P. D. Wilson)—*Bone tumor, giant cell, radius, lower end, recurrent, dead of cardiac failure at 70 years*

*History*—Mrs K., a white woman aged 68, a patient of Dr P. D. Wilson, Boston, complained of pain and aching in the wrist of two or three months' duration, beginning in April, 1920. The pain was worse on motion.

*Examination and Course*—The lower end of the forearm was swollen chiefly on the radial side and on the dorsum. On March 23, 1922, roentgen examination showed the bone shell almost completely destroyed and no trabeculae. On June, 1923, examination revealed complete destruction of the lower part of the radius. The first operation was performed on July 29, 1920. Partial curettement was performed. A putty-like material was removed. Bleeding was profuse. The wound was packed with gauze and drained, and roentgen treatment was begun. On Nov. 30, 1920, the second operation was performed by Dr. Simmons and Dr. Wilson. Tissue like current jelly was curetted. There was no chemical or thermal cauterization at either operation. Radium seeds were placed in the cavity and radium tubes at the wound entrance. On March 2, 1922, curetting was done and roentgen treatment was administered. On July 23, 1922, curetting was again performed. On Sept. 23, 1922, the arm was amputated.

The specimen removed at the first operation showed typical giant cell tumor. The condition was diagnosed by Dr. Bloodgood. The specimen removed at amputation revealed marked fibroblastic proliferation. The condition was diagnosed sarcoma by many pathologists. On Oct. 23, 1922, the condition recurred in the stump. On Nov. 23, 1922, the patient complained of pain in the back. On Dec. 23, 1922, two years and eight months after the first symptoms occurred, the patient died of pneumonia (probably pulmonary metastases?) and cardiac failure.

*Comment*—The original tumor was unquestionably a benign giant cell tumor of which sections are available (fig. 1). Repeated recurrences can be ascribed to partial curettement in the first instance, the age of the patient and the marked destruction of the shell of cortical bone. The sections from the amputated specimen did not show sarcoma, but a marked "healing reaction" characterized by a proliferation of fibroblasts (fig. 21). Death was the result of pneumonia and cardiac failure. It should be noted that roentgen treatment after the first curettement did not prevent recurrence.

It will be seen that the patient in case 1 reported by Turner and Waugh was shown at autopsy to have died of pulmonary embolism. The so-called venous metastasis was likewise a small embolus in the vein, containing giant cell tissue, followed by thrombus formation as reported by Bloodgood after examination of the sections sent to this laboratory. The patient in case 2, registered by Dr. P. D. Wilson with the Bone Registry of the American College of Surgeons showed a primary tumor of the typical giant cell variety and a secondary change after four curettings and roentgen and radium therapy characterized by an abundance of young proliferating fibroblasts. The cause of death

on further investigation proved to be cardiac decompensation with dyspnea and edema, followed by pneumonia, in a woman, aged 70

In brief, these two cases were both in adults over 40, occurring in the lower part of the femur and in the lower end of the radius. The first did not recur, but the second recurred repeatedly owing to incomplete primary curetting, the destruction of the bone shell and to the fact that the age of the patient was beyond the time when the healing power of the bone cell is capable of effective effort

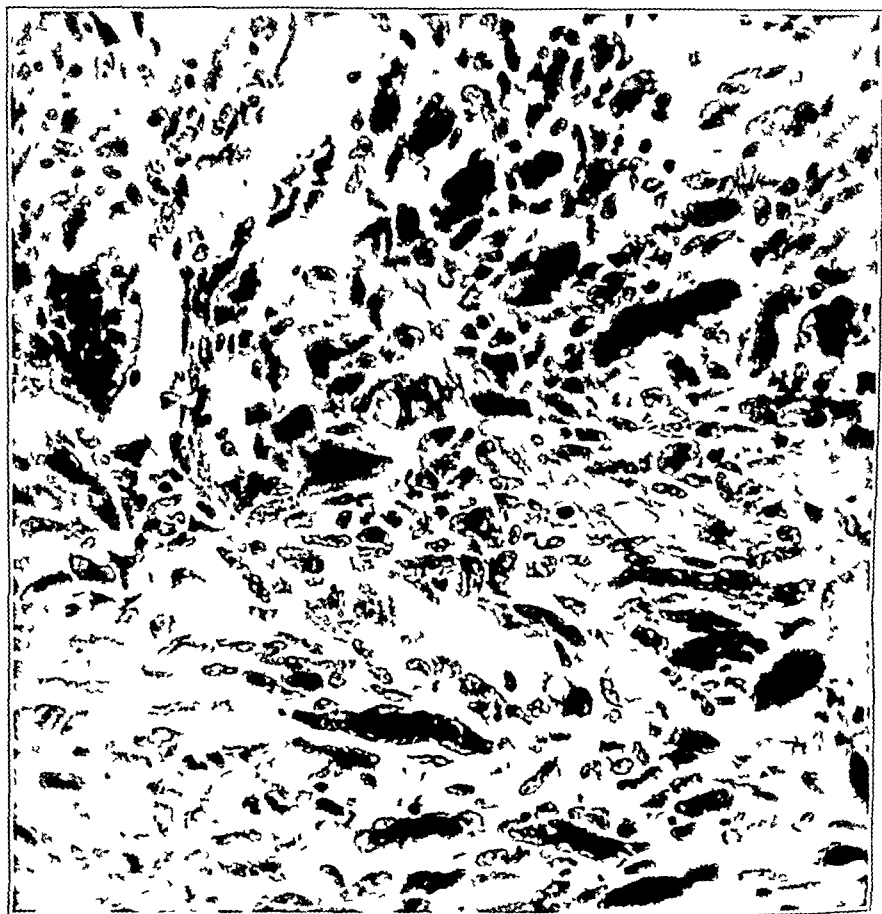


Fig 17 (P N 40766 metastatic case 3 of Dr J L Goforth) —High power photomicrograph showing a giant cell area bordering on osteogenic sarcoma. Sections for photomicrography forwarded to the authors through the courtesy of Dr Goforth (specimen illustrated is from third operation)

In group 2 there are four cases, clinically similar which include those reported by Dr Goforth,<sup>2</sup> Dr Finch and Dr Gleave, Dr Chatterton and Dr Flagstad, and one recorded in this laboratory by Dr Dean Lewis

CASE 3 (P N 40766, figs 17 and 18, Dr J L Goforth, case 5) —*Bone tumor, giant cell (?), tibia upper end, left, recurrent and metastatic*

*History*—L G, a white man aged 34, a patient of Drs Cooperman and Case, was admitted to the Polyclinic Hospital, Philadelphia, with the complaint of trauma to the left knee one year previously (1916) and pain and swelling of three or four months duration

*Examination and Course*—Roentgen examination in 1921 (before amputation), showed all the bones at the knee joint involved bone destruction and bone formation, the bone shell of the tibia gone and joint involvement (resembled sclerosing sarcoma—Bloodgood)

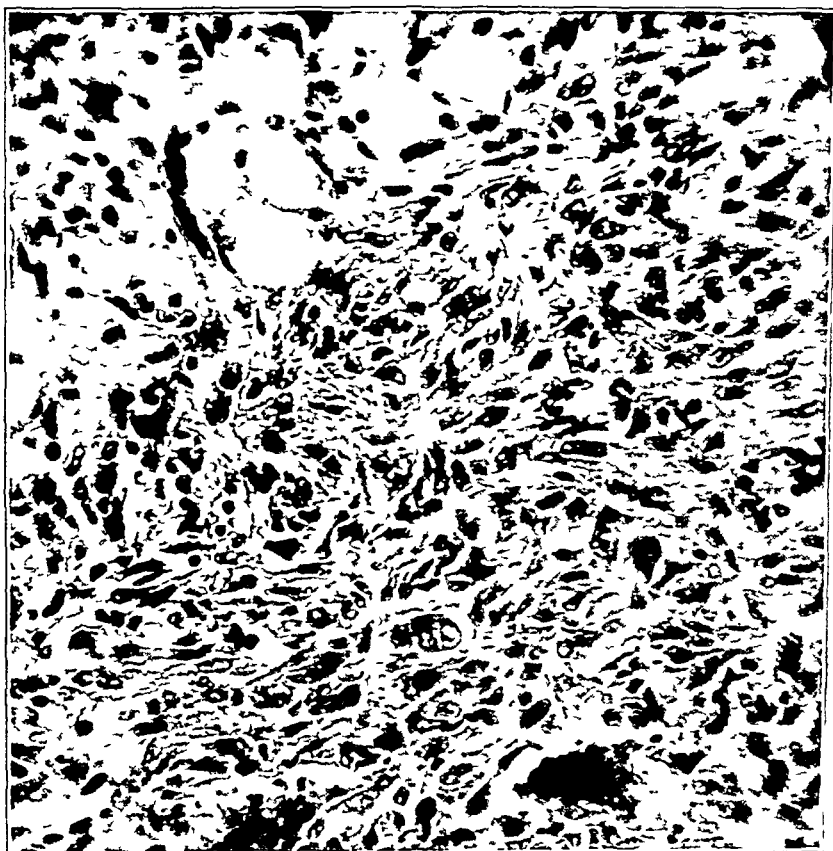


Fig 18 (P N 40766, metastatic case 3 of Dr J L Goforth)—Same tumor as shown in figure 17 The picture shows a cluster of foam cells occurring in osteogenic sarcoma This tumor had perforated into the soft parts and metastasized

Thorough curettement was done in 1917 followed by recurrence In 1919 a second curettement was done with no cauterization again followed by recurrence The patient used braces and crutches for ten months In October 1921, the leg was amputated above the knee

No tissue was preserved from the first or second curettements Tissue taken from the amputated specimen showed areas of true osteogenic sarcoma along side of areas of giant cell tissue (Bloodgood) In August 1922 metastases to

the chest were shown by roentgen examination. Death occurred in November, 1922, six years after injury. Autopsy was not performed.

*Comment*—Dr Goforth agreed that the weak point in this case was the absence of tissue or sections from both the first and second operations. There is, therefore, no proof of the identity of the first tumor. The amputated specimen shows sarcoma. The time elapsing before amputation would permit secondary sarcoma in an unhealed lesion. There is also possibility of a slowly progressive sarcoma from the first.

CASE 4 (P N 40768, fig 19, Dr Finch and Dr Gleave<sup>8</sup>)—*Bone tumor, giant cell (?), femur, lower end, right, metastatic after exploration and two pathologic fractures, recurrence in stump after amputation*

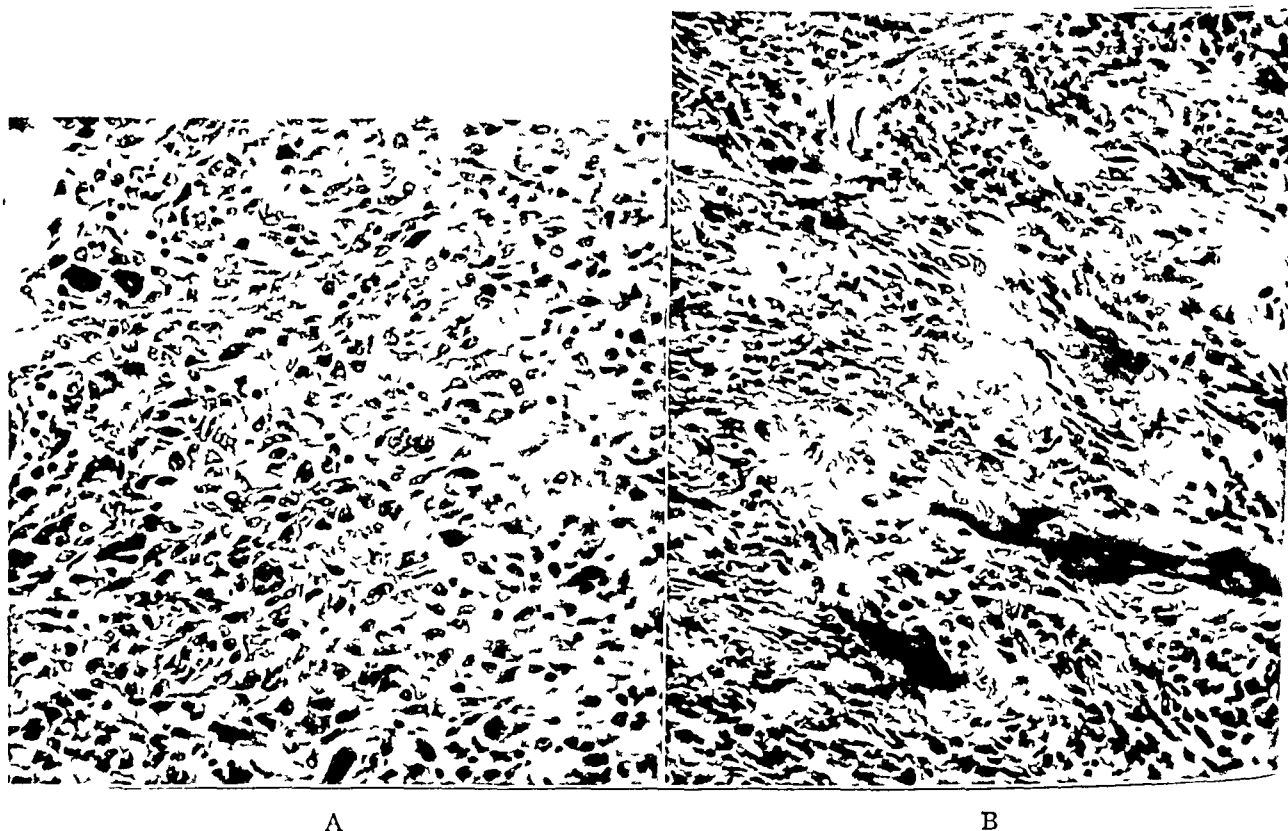


Fig 19 (P N 40768, metastatic case 4 of Dr Finch and Dr Gleave)—*A* Photomicrograph of a sarcomatous nodule in the lung showing small giant cells of the type frequently occurring in osteogenic sarcoma and atypical of benign giant cell tumor. Sections for photomicrography forwarded to the authors through the courtesy of Dr Finch and Dr Gleave. *B* Photomicrograph of a sarcomatous nodule in the lung showing bone formation of tumor origin. This demonstrates conclusively that the metastasizing lesion was osteogenic sarcoma.

*History*—W B, a white man aged 49, a patient of Drs Finch and Gleave entered the Royal Infirmary, Sheffield, England, complaining of pain in the right knee in 1915, injury to "ligaments" in 1916, pathologic fracture in March, 1917 which healed after exploration and treatment, pain and swelling in 1919. In 1921

giant cell tumor was diagnosed, the original diagnosis being revised. There was recurrent pain in December, 1924, and a second pathologic fracture in January, 1925.

*Examination and Course*—In January, 1925, roentgen examination showed the bone shell perforated, fracture and some new bone formation (Gross specimen showed perforation of shell and much destruction of bone). The first operation was performed on March 24, 1917. The site of the pathologic fracture was explored. The condition was diagnosed osteitis deformans. The fracture healed. The second fracture occurred on Jan 18, 1925. On Jan 21, 1925, a mid thigh amputation was performed. In July 1925, the sputum was blood stained. Recurrence in the stump occurred on Oct 2, 1925.

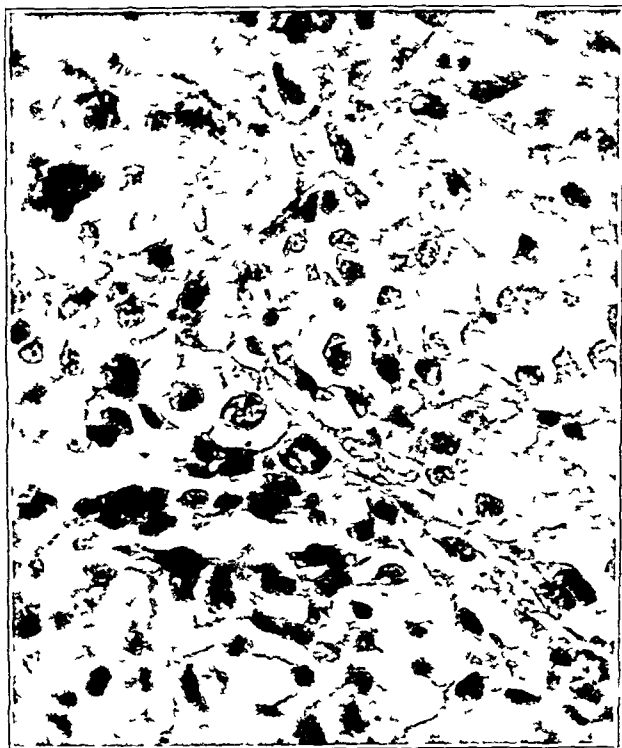


Fig 20 (P N 40874, metastatic case 5 of Dr C C Chatterton and Dr A E Flagstad)—High power photomicrograph of a section from the tissue of the second operation. Microscopically, this tumor must be classed as a form of chondroblastic sarcoma. Material for photomicrograph was made available through the courtesy of Dr Chatterton and Dr Flagstad.

No microscopic report on the tissue taken from the original tumor was available (Recurrence in stump and lung metastasis—sarcoma—Bloodgood). On Jan 30 1926, eleven years after the first symptoms, the patient died. Autopsy showed metastatic nodules in the lungs.

*Comment*—There is no pathologic report on the first operation in March 1917. Sections from the amputated specimen in 1925 showed sarcoma. There is no

proof, therefore, of the nature of the primary tumor. Nearly eight years elapsed before amputation. There was ample time for a secondary growth to arise at the unhealed site.

CASE 5 (P N 40874, fig 20, Dr C C Chatterton and Dr A E Flagstad, case 1<sup>23</sup>)—*Bone tumor, giant cell (?) , femur, lower end, left, recurrent and metastatic*

*History*—A white woman, aged 30, a patient of Drs Chatterton and Flagstad, was first seen on Dec 4, 1920, complaining of pain of five years' duration (since 1915), and swelling for two years (since 1918). In June, 1920, a pathologic fracture had occurred. Crutches were used thereafter. There was limitation of motion at the left knee.

*Examination and Course*—In December, 1920, roentgen examination revealed an old fracture, a shell perforated and a trabeculated area of bone destruction (Chatterton and Flagstad thought bone shell intact). On Oct 10, 1923, before amputation, there was complete destruction of the area about the old fracture with little new bone formation. On Dec 5, 1920, curettement (partial) was performed. Cauterization was done with phenol and glycerin, and a cast was applied. Pain returned during September, 1923. On Oct 15, 1923, the leg was amputated at the mid thigh because of severe pain and fracture.

Microscopic examination of the amputated specimen of the recurrent tumor showed a condition diagnosed sarcoma (no note as to who diagnosed original sections). On Nov 23, 1923, there was pleural effusion. Bloody fluid was withdrawn by thoracentesis. On Dec 4, 1923, eight years after the first symptoms, the patient died.

*Comment*—There is no proof of the nature of the original tumor. As the authors state "Error in diagnosis at biopsy in 1920 must be granted because the slides and gross (specimen) have been destroyed." The length of the clinical course suggests that either a low grade sarcoma or more likely a secondary growth at the site of the unhealed primary tumor may have accounted for the death of the patient.

CASE 6 (P N 31890, figs 21 and 22, JCB N 12425, Dr Dean Lewis)—*Bone tumor, giant cell (?) , tibia, lower end, left, recurrent and metastatic*

*History*—C S, a white man, aged 35, patient of Dr Dean Lewis, complained of swelling and pain in the leg of seven months' duration. The tumor recurred thirteen months after curettement. Roentgen examination showed a central, bone-destructive lesion of the epiphysis, of the lower end of the tibia. The first operation was performed by Dr Lewis in 1908. Curettement was performed. The tumor recurred in the tibia about 2½ inches above the original site. The second operation was done by Dr Lewis in November, 1909. Amputation was performed.

Sections from the original curetting and from amputation were lost. Dr Lewis said that he believed the condition was typical giant cell tumor. Sections from autopsy, Aug 1, 1916, following metastases to the lungs showed osteogenic sarcoma with giant cell areas, bone lamellae and bone marrow.

The patient died in August, 1916, eight years and seven months after the first symptoms. Metastases to the lungs were demonstrated at autopsy.

*Comment*—All data and specimens relating to the original tumor have been lost. Dr Lewis states that he has never reported the case for this reason, although he believes the initial lesion to have been a giant cell tumor. Although

the amputation was performed in 1909 the patient lived for seven years thereafter suggesting the possibility of a slowly growing sarcoma

In this group two of these tumors were in the femur and two were in the tibia. All of these tumors recurred after initial operation in all cases the patients were over 30 years of age at the time of amputation and in each case amputation was followed by pulmonary metastases either clini-

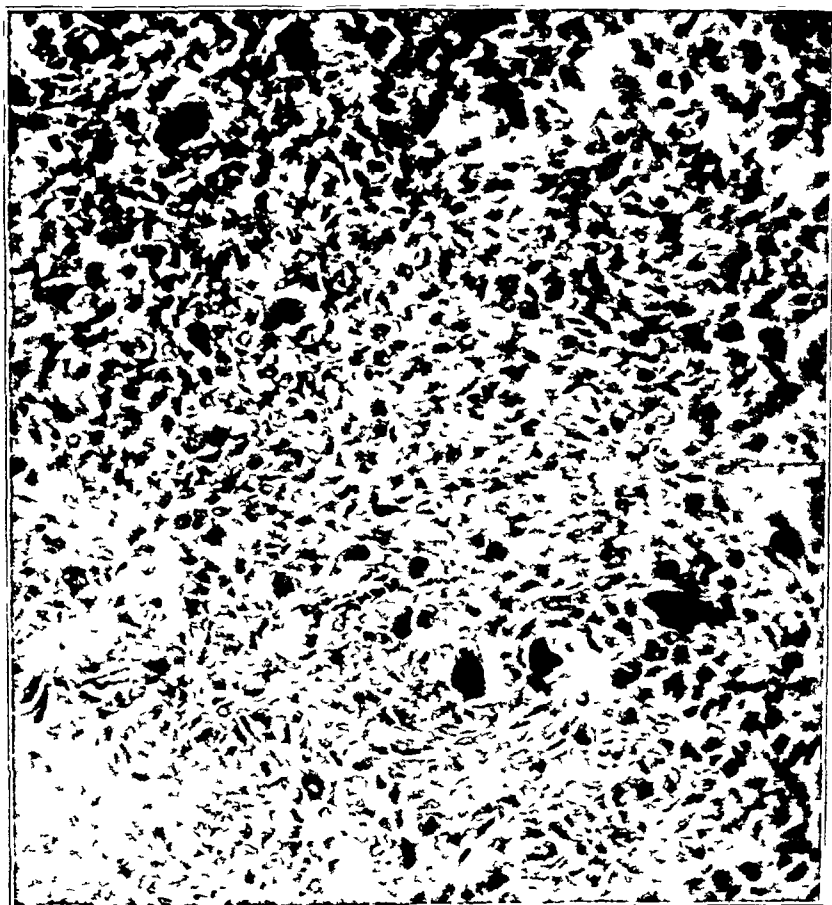


Fig 21 (P N 31890 metastatic case 6 of Dr Dean Lewis) —The photomicrograph shows a metastatic nodule in the lung with small giant cells typical of osteogenic sarcoma. The cellular stroma of the tumor is also characteristic of an early phase of osteogenic sarcoma.

cally or microscopically demonstrated. In all of these cases the duration of the interval between the first symptoms and death was over six years, and in no case was the material from the original lesion preserved so that microscopic confirmation of the nature of the primary growth could not be carried out at the time of reporting the case. The nature of the



recurrent growth giving rise to the metastases, however, has been studied by us in each instance, and is unquestionably osteogenic sarcoma. In these four cases, therefore, we have a primary lesion of the leg, of undetermined microscopic nature, unsuccessfully treated giving rise—after an interval of years—to a metastasizing bone lesion. The long interval of time consumed by the clinical course of these growths suggests that two separate bone lesions, one superimposed on the other accounted for



Fig 22 (P N 31890, metastatic case 6 of Dr Dean Lewis) —Another portion of the same metastatic lung nodule shown in figure 21. Here the tumor has progressed to mature bone formation showing highly developed bony lamellae and actual cellular bone marrow. This highly differentiated structure is most unusual in osteogenic sarcoma, and must be attributed to the slow growth of the nodule which was excised at the autopsy table six years and nine months after the original tumor had been amputated from the leg. This sarcomatous nodule in the lung was, therefore, of approximately seven years' duration.

the manifestations observed. The important point to be emphasized is that sarcoma arose in a bone at the site of a previous lesion that had failed to heal and that had been subjected to trauma and to unsuccessful operative procedures. Failure to heal can be attributed to the age of the

patients (over 30) and to the mode of treatment instituted. The fact that sarcoma eventually arose at these sites has no bearing on the relation of the original lesion to the sarcoma, for squamous cell carcinoma has been known to occur in a draining sinus of chronic osteomyelitis for which the patient has been unsuccessfully treated, and we have observed such carcinoma in the unhealed sinus of a giant cell tumor curetted ten years previously. No one would claim that the giant cell tumor in this case underwent carcinomatous transformation. Thus in group 2 we have four cases of osteogenic sarcoma arising secondarily at the sites in bone which were the seats of unhealed previous lesions. The nature of the original lesion is not known with certainty. In one case osteitis deformans was suspected at the time of exploration. In the other cases benign giant cell tumor was suspected.

Since sections from the original lesions are not available for microscopic study, the possibility of a slowly growing sarcoma, present from the first, must be considered. In this connection it is significant that the form of osteogenic sarcoma present in these cases of recurrent lesions resembles a type of fibroblastic origin, which is usually slowly fatal and occurs generally in patients over 30, as shown by a study of over fifty cases to be reported later.

In group 3 there are two cases, one reported by Drs. Stone and Ewing, and recorded in this laboratory by Dr. T. A. Dingman.

CASE 7 (P. N. 40872, fig. 23, Dr. Martin, Dr. Coley, Dr. Stone, Dr. Ewing)  
—*Bone tumor, giant cell (?) , tibia, upper end, right, recurrent and metastatic*

*History*—J. N., a white man, aged 19, a patient at St. Luke's Hospital and Memorial Hospital, New York City, noticed swelling, tenderness and pain in February, 1919. No history of trauma was given.

*Examination and Course*—On June 29, 1919, roentgen examination revealed the bone shell intact and a central area of bone destruction. The first operation was performed in February, 1919, curettement and cauterization with phenol being done. In July, 1919, the second operation was performed, and 47 millicuries of radium emanation was placed in the cavity for forty-eight hours. There was a sinus during the winter and fall of 1919. It gradually healed without infection. In April, 1920, the sinus began to discharge. On June 4, 1920, curettement was followed by osteomyelitis. On June 30, 1920, amputation was performed. Microscopic section from the original tumor was pronounced benign giant cell tumor by Drs. Bloodgood, Wolbach, Mallory and Stewart of Leeds. Drs. Wood, MacCarty and Broder diagnosed the condition a malignant growth. Tissue from the amputated stump showed sarcoma.

In January, 1921, metastasis to the lungs was shown by roentgen examination. The patient died on March 13, 1921, two years and one month after the first symptoms.

*Comment*—The age of this patient and the short clinical course suggest osteogenic sarcoma of the "chondroblastic" type which frequently shows a resorptive giant cell phase. The sections sent to us resemble this type of sarcoma, as do the sections from the amputated specimen. For comparison with thirty-two other sarcomas of this type see section IV.

CASE 8 (P N 35226, fig 24, JCB N 13714, Dr Dingman) —*Bone tumor, giant cell tumor (?), femur, left, inner condyle above epiphysis, recurrent and metastatic*

*History*—E T, a white man, aged 16, a patient of Dr T A Dingman, Paterson, N J, struck his knee on the floor while playing basketball five weeks previously. The knee became sore and painful after a week.

*Examination and Course*—Examination revealed slight swelling and definite tenderness over the mesial side at the inner condyle of the left femur. No fluid

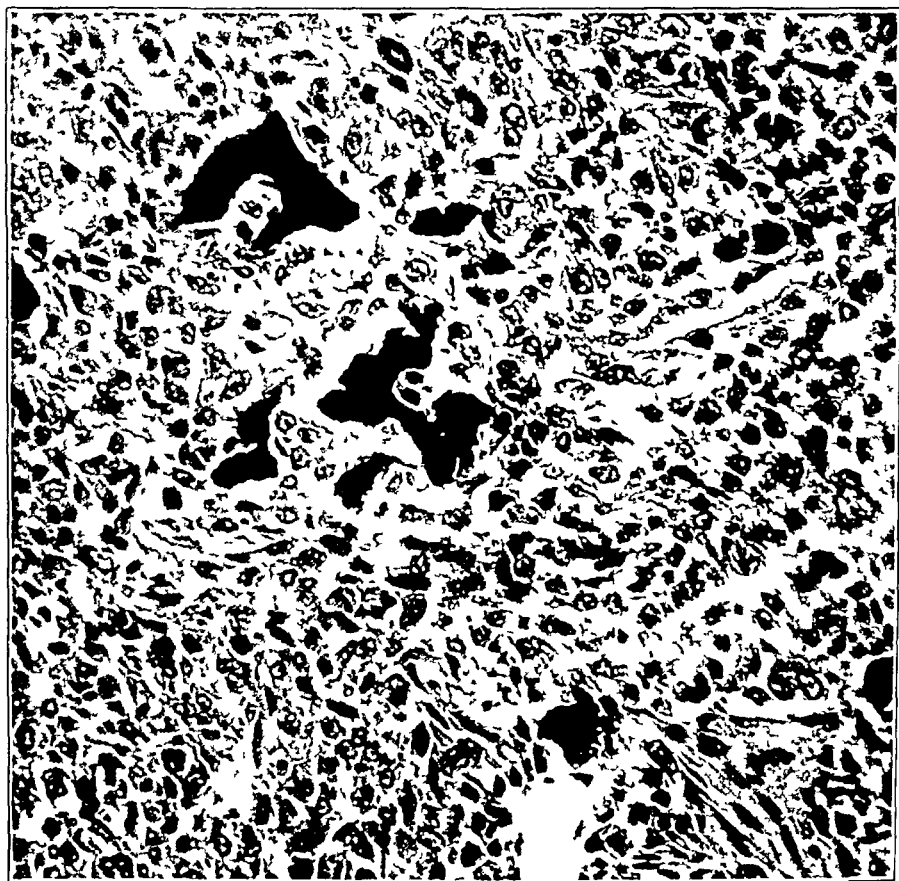


Fig 23 (P N 40872, metastatic case 7 from Dr Stone and Dr Ewing) — Specimen from the fourth operation. The microscopic structure shown is that of the chondroblastic form of sarcoma illustrated in figures 14, 15, 20 and 24. Photographs reproduced from the article of Dr Stone and Dr Ewing through the courtesy of Dr James Ewing.

was present. Roentgen examination showed an area of bone destruction beneath the cortex with overlying periosteal reaction. The first operation was performed by Dr Dingman on April 4, 1924, curetting and cauterization with phenol being done. A second operation was performed by Dr Dingman on April 19, 1924. The old wound was reopened and cauterization was done with electricity. On June 8, 1924, the leg was amputated by Dr Dingman at the mid thigh. There was no recurrence in the stump.

Tissue taken at the first and second operations showed typical giant cell tumor, but very cellular (diagnosed by Dr Bloodgood 1924). The amputated specimen showed sarcoma with altered giant cells. On August 16, bloody fluid was obtained by thoracentesis. In September 1924, on roentgen examination metastases were seen to the lungs and pleura. The patient died in September, six months after the injury.

*Comment*—As in case 7, the clinical course and age suggest sarcoma. Restudy of the sections show 'chondroblastic sarcoma (section IV).

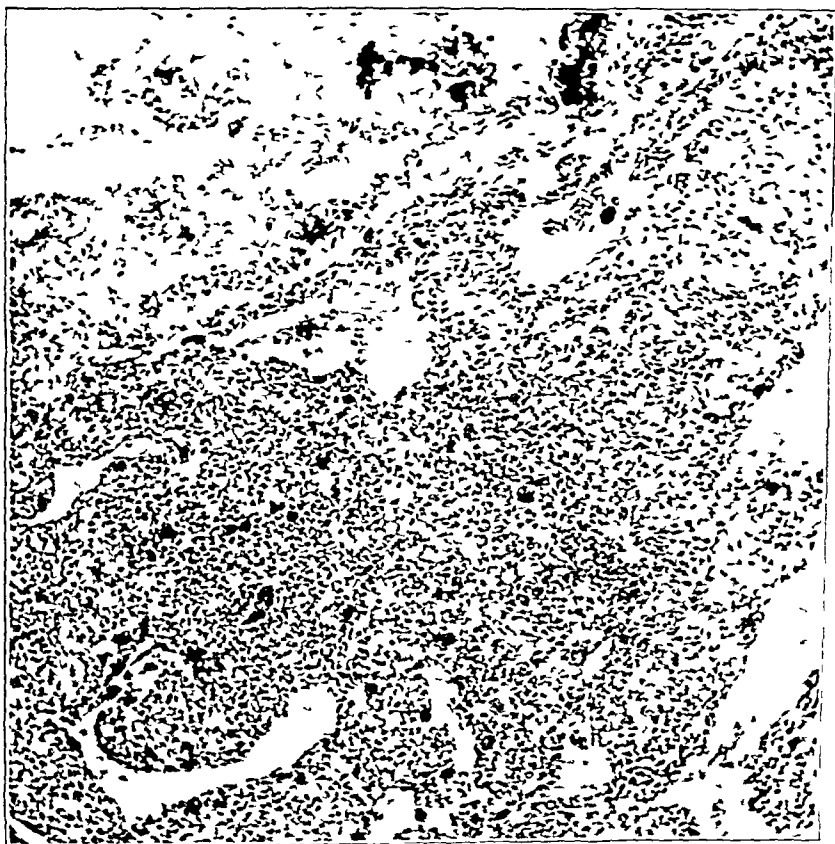


Fig. 24 (P. N. 35226, metastatic case 8 of Dr Dingman)—Low power photomicrograph showing a chondroblastic sarcoma undergoing calcification and subsequent vascularization with giant cell invasion. Sections from this case were originally diagnosed giant cell tumor, but the patient died six months after the initial symptoms. The section illustrated is from the second operation.

Clinically, these two lesions have much in common. Both occurred about the knee joint, the upper part of the tibia and the lower part of the femur. In contrast to the other six cases the two growths were in young men, from 16 to 19 years of age—the period of the maximum proliferative power of the bone cell—the sarcoma age. In both instances the course was relatively brief with two or more unsuccessful curettings.

preceding amputation, with death by metastases in less than a year after amputation in each case. The two cases also present a similar microscopic picture. The sections show areas of round and stellate chondroblasts with a minimum amount of calcified matrix. In the vascular regions neighboring the calcified areas, giant cells are present representing the typical resorptive phase about calcified cartilage—in these instances in an abortive and malignant form. As was shown by an analysis of osteogenic sarcoma (in a forthcoming article), this type of “chondroblastic sarcoma” is frequently mistaken for other types of bone tumors, namely, round cell sarcoma of bone and giant cell tumor. In these two cases it is felt that the original lesion was a form of osteogenic sarcoma, and not giant cell tumor.

We may conclude from an analysis of these eight cases selected as avowedly metastatic from among hundreds of typically benign giant cell tumors that they are not strictly bona fide. In no case has transformation of giant cell tumor into sarcoma been proved, and in no case have typical giant cell tumor nodules been found as metastases in the lungs. In half of the cases a diagnostic error was made, either in ascribing death from other causes erroneously to metastases, or in failing to recognize the histology of the original lesion as sarcoma. In the other four cases, since material from the original lesion was not saved for confirmation of the diagnosis, there is no proof that the original tumors were typical giant cell tumors, and not a low grade malignancy from the start, nor can it be contended that the giant cell areas in the final sarcomatous growths were other than a resorptive phase in osteogenic sarcoma without histologic connection with giant cell tumor. The only plausible deduction is that in a few isolated instances an apparently benign lesion of bone, when subjected to unsuccessful treatment and to trauma, may by its failure to heal, provide a fertile site for the subsequent development of osteogenic sarcoma. The unhealed area of bone, and not the nature of the original lesion is the important factor.

#### IV OSTEOGENIC SARCOMA WITH GIANT CELLS

Although osteogenic sarcoma represents the largest and perhaps the most complex group of tumors of the bone, and cannot be dealt with adequately here, still for the purpose of clarifying some of the conclusions set forth thus far, we shall anticipate briefly certain of the results of a study of these lesions to be published later, particularly those pertaining to osteogenic sarcoma with giant cells. In spite of the “consolidating” efforts of the Bone Registry and recent publications<sup>14</sup> endorsed by the American College of Surgeons, we are compelled to recognize on embryologic, histologic and clinical grounds, two broad and

<sup>14</sup> Kolodny, A. Bone Sarcoma, Chicago, Surgical Publishing Company of Chicago, 1927.

well defined groups of osteogenic sarcoma—the chondroblastic and the fibroblastic series

As would be expected on biologic grounds the more primitive type of chondroblastic bone formation gives rise to a more malignant and rapidly growing form of osteogenic sarcoma while the fibroblastic series which differentiates the osteoblast or permanent bone builder, has a longer average clinical course and a higher percentage of five year cures

Giant cell areas are not primarily characteristic of either type of osteogenic sarcoma but may be found in both. In the slower growing fibroblastic type of osteogenic sarcoma particularly in those cases in which operation has been performed unsuccessfully and in which there have been recurrences loci of necrotic bone will be present and giant cells on a phagocytic errand will invade the tumor. More frequently the presence of many small giant cells in these tumors is to be explained by a chemotaxis of these phagocytes to the collagen proliferated by these tumors which acts as a foreign body. The abundant sarcomatous tissue with immense plump spindle cells containing vesicular and hyperchromatic nuclei should prevent confusion in making the diagnosis

As will be gathered from the foregoing discussion of the malignant variants, and metastatic groups, it is a chondroblastic form of osteogenic sarcoma which more often leads to confusion in microscopic diagnosis (fig 14). Four tumors classed as either malignant variants or metastatic giant cell tumor were found erroneously labeled as giant cell in origin and were rediagnosed as a form of chondroblastic sarcoma. When we compare these four tumors with twenty-nine other cases with similar clinical and microscopic features among the sarcomas, we find such a rediagnosis amply justified

Reviewed as a single group, these thirty-three cases present remarkably uniform features. With three exceptions all occurred within the narrow age limits of from 14 to 20. Also with three exceptions, all are in the lower extremities with a period of symptoms averaging less than six months, and an average duration of life after operation of less than eleven months. Two of the four living patients have survived curettage eight and a half years and one year respectively. The other two are living, twelve and four months after amputation. Hence we can say that clinically this is a most rapid and malignant form of tumor

On roentgen examination the lesion generally shows a central area of bone destruction near an epiphysis with an early periosteal reaction (fig 13). Under the microscope there is seen an assortment of polyhedral and angular cells with large well defined nuclei which are in reality chondroblasts. This is proved by scanty areas of typical cartilaginous matrix laid down in a scattered fashion here and there undergoing calcification—an abortive attempt at producing temporary or substitution bone. When occasional areas of this abortive calcified cartilage are being vascularized and resorbed by giant cell osteoclasts

according to the usual embryologic process for substitution bone, the giant cell tumor will be simulated. It is just such areas that lead to an erroneous diagnosis of giant cell tumor, readily corrected by examination of the chondroblastic areas with small foci of calcified and uncalcified matrix. Here the malignant phase of the tumor is the rapidly proliferating chondroblast, which rarely reaches in even an abortive form the stage of calcified cartilage. The healing or reactive phase is represented by the attempt on the part of the normal bone to resorb the calcified cartilage by osteoclastic proliferation (giant cell areas) preparatory to filling in with compact "fibroblastic" bone.<sup>15</sup> Unfortunately, such a healed stage is never reached, but the pathologist may see just enough of the reactive giant cell phase to diagnose the lesion incorrectly as giant cell tumor.

TABLE 4—*Summary of Treatment in Two Hundred and Fourteen Cases of Giant Cell Tumor*

Primary amputations	30 cases
Primary resections	34 cases
Curetting only	71 cases
Repeated curetting for recurrence	16 cases
Curetting plus amputation for recurrence	5 cases
Curetting plus resection for recurrence	10 cases
Curetting plus amputation for infection	3 cases
Resection plus amputation	2 cases
Exploration only	13 cases
Operation refused	9 cases
Roentgen therapy only	5 cases
No treatment recorded	16 cases
Total number of cases	214 cases
Total curettings	105 cases
Recurrent cases	31 cases
'Metastatic' cases not included in above	8 cases

## V THE TREATMENT OF GIANT CELL TUMOR

Since the effective contributions of Bloodgood to the American literature of giant cell tumor in 1910 and 1912,<sup>16</sup> the progress in treatment has been steadily toward increasing conservatism. Amputation, then resection and then curettement have prevailed as the treatment of choice, and now roentgen therapy alone is being advocated by some. The 214 cases forming the basis of the present study depict this evolution in treatment, these cases recording the various forms of therapy practiced since 1896 (table 4).

15 We believe this view, that the giant cell areas in chondroblastic sarcoma are a product of normal reacting bone, nearer the truth than the supposition that they are a further stage in the malignant osteogenesis of cartilaginous bone by the sarcomatous chondroblasts. Since we can observe the death of the chondroblasts with the formation of the calcified matrix, we do not see how they could survive to initiate the giant cell phase, as a further malignant product. The fact that giant cells are more numerous at the tumor margin at the site of normal reactive bone also supports this view.

16 Bloodgood (footnotes 4 and 11)

*Primary Treatment*—Among the primary forms of treatment are listed amputation resection, curettement exploration only, roentgen therapy only and no treatment by the physician. Of these various forms, curettement has been used most frequently, although apparent cures have resulted in all six types listed. Excluding the alleged metastatic group and a few isolated giant cell tumors of the skull and vertebrae (dangerous because of location) mortality either from treatment or from the tumor itself has been exceedingly rare indeed—less than 1 per cent.

Amputation was the primary operation in thirty cases and although one third of these cases were explored before amputation, and twenty had shown perforation of the bone shell prior to operation, there were no recurrences, no operative deaths and no patient died of tumor. In half of these cases the patients have remained well from ten to twenty years and over, but in spite of these uniformly good results, the sacrifice of the limb in the first instance is rarely justified. Hardly ever is the lesion so advanced that the function of the limb is beyond restoration, and even when pathologic fracture has occurred, it must be remembered that the majority of these heal with appropriate treatment. Particularly in the upper extremity the conservation of the limb or even one of its minor members is worthy of trial.

Resection was performed as the initial procedure for relief in thirty-four cases. There were no deaths from either the operation or the tumor, and if we except an excision of a tumor in the lower jaw, recorded as resection, and a similar case in the radius, there was not a single recurrence. In five cases a portion of the bony shell was destroyed before operation, in three pathologic fracture had preceded, and in three other cases, there had been previous exploration. Here again the mode of treatment was usually needlessly radical, and in five cases involving the tibia and two involving the femur in view of the functional results, curettement followed by cauterization would have been preferable. Preliminary roentgen therapy was not resorted to in a single instance in this group, and in many, the age of the patient and the extent of preservation of the bone shell favored treatment by curettage. Resection is permissible, it would seem, in advanced cases or in cases of elderly persons with involvement of the fibula, radius or ulna, although in eleven cases in the ulna, in which the patients were treated by curettement, there was not a single recurrence.

In 105 cases primary curettement was the mode of treatment. The condition in thirty-one of these cases recurred (tables 1 and 2). One patient died of a tumor in the vertebrae and another grew progressively worse after partial curettement of a giant cell growth in the sphenoid bone. Seven patients became secondarily infected after the first or



second curettement, necessitating amputation in three instances. Several of these infections followed radium implantation into the wound, a postoperative procedure which has been proved to be ill advised in this group of tumors. Although it cannot be determined from the records in exactly how many instances, thermal or chemical cauterization followed

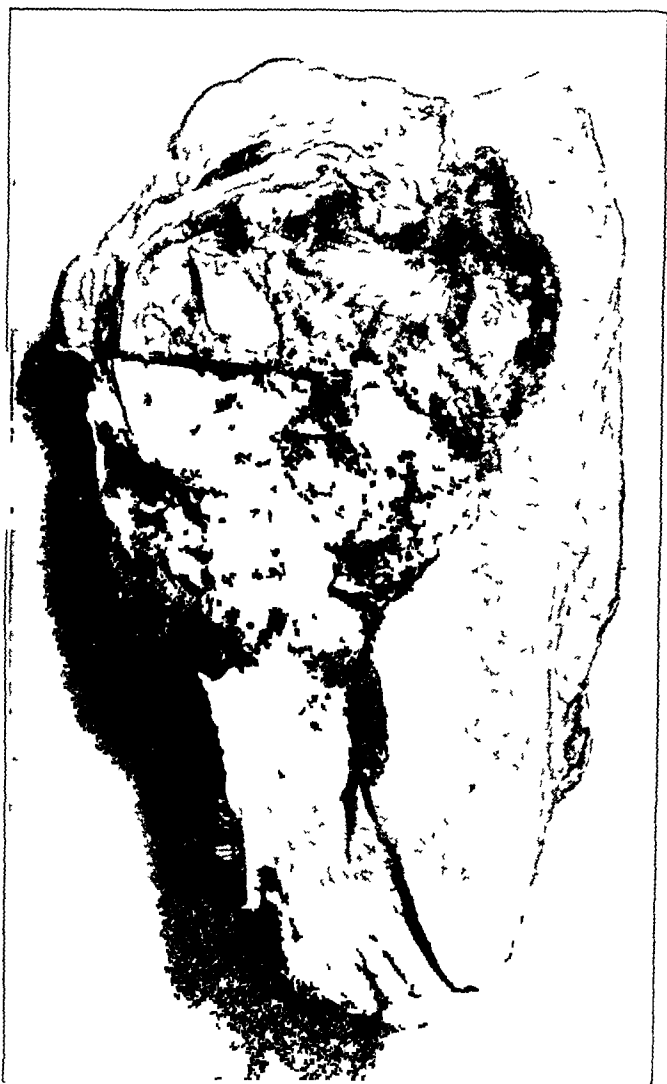


Fig 25 (P N 26091) —Gross specimen of a giant cell tumor amputated after two unsuccessful curettings. Note the destruction of cortical bone at one side of the tumor.

curettement, it can be safely stated from this study that recurrence was more frequent in the group in which no cauterization was employed. In view of this fact, and in consideration of the fact that the patients in sixteen of the thirty-one recurrent cases were cured by a second or even third curettement, it may be stated that curettement properly per-

formed<sup>17</sup> in carefully selected cases is unquestionably the treatment of choice (figs 25 and 26)

Primary roentgen treatment without operation was employed in five cases—three have been followed and are living less than five years, this mode of therapy being too recent to judge at present in regard to the ultimate result in these cases<sup>18</sup> When postoperative roentgen treatments have been given in certain instances they have not prevented recurrence and would seem to be of no particular benefit As Bloodgood has pointed



Fig 26—Photomicrograph made from section taken from the specimen shown in figure 25 This giant cell tumor has not altered its typical structure despite the two previous operations

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17 The method advocated by Bloodgood consists of thorough curettage followed by cauterization with pure phenol subsequently neutralized by 95 per cent alcohol A 50 per cent zinc chloride solution is finally applied The electric cautery or soldering iron may be substituted for chemical cauterization.

18 In a case recently observed in a woman, aged 31, preliminary treatment had been given for six weeks for a giant cell tumor of the lower part of the radius with intact bone shell When seen by one of us (C F G), the tumor had advanced, completely destroying the shell of bone the lesion having been uninfluenced by the roentgen treatment

out, roentgen therapy, when compared to proper curettement, is more uncertain, often more prolonged, and does not offer the benefits of microscopic diagnosis in doubtful cases

Nine patients refused operative treatment, and of these, seven cases have been followed—two are dead (one of hemorrhage), three are living over five years and two are well less than five years. Here there is a considerable risk of either crippling or death, and prompt treatment in view of the good results obtained in the majority of cases would have offered much to these misguided patients had they availed themselves of surgical service.

*Secondary Treatment*—When curettement or excision has been followed by recurrence, the problem of the secondary treatment of giant cell tumor arises. Experience shows that little can be expected from roentgen therapy and more undesirable results may follow radium implantation into the wound. If sections or tissue are available from the original operation, they should be submitted to a competent pathologist for confirmation and check on the diagnosis of the primary growth. If not, the recurrent tumor should be reoperated on when there is an opportunity for one familiar with the microscopic appearances of this group of lesions to pass on the frozen sections at the time of operation. In any event, an attempt should be made to reevaluate the benign or malignant character of the growth. If the recurrence is benign giant cell tumor, further curettement may be tried if the lesion is in the femur or tibia, and if the age of the patient and the degree of preservation of the bone shell warrant it. In the fibula, radius, ulna or humerus, resection is advised.

Should the lesion be rediagnosed sarcoma, amputation followed by deep roentgen ray is warranted, since one five-year cure in this series was apparently achieved under such conditions. The crux of the matter, of course, lies in an accurate pathologic diagnosis.

#### SUMMARY

Forty-one cases of giant cell tumor showing clinical or microscopic evidence of malignant tendencies have been analyzed. In the clinical group, twenty-six cases recurring after primary curettement were studied. Recurrence in this group was found to depend not on histologic structure, but on a poor selection in the type of treatment applied in the individual case or on an incomplete operation. Advanced destruction of the bone shell, incomplete curettement, failure to use chemical or thermal cauterization or needless sacrifice of cortical bone at the operation, as well as an age over 35, were found to be factors predisposing to recurrence after curettement.

In seven cases showing a microscopic resemblance to malignancy, the histologic change was usually found to be the result and not the cause

of the recurrence being dependent on intervening infection, necrosis or an accentuated healing reaction following irradiation. In two cases, actual sarcoma with giant cells were found to be erroneously placed in this group.

Eight cases of so-called metastatic giant cell tumors collected from the literature and from the surgical pathological laboratory of the Johns Hopkins Hospital have been reviewed and abstracted. In no case were the metastatic nodules in the lungs composed of typical giant cell tumor, and in no case was an original tumor of proved benign giant cell structure found associated with death from metastasis. In four of the cases a diagnostic error was made either in ascribing death from other causes erroneously to metastases or in failing to recognize the histology of the original lesion as sarcoma. In the other four cases, material from the original lesion was not saved for confirmation of the diagnosis—and therefore the possibility was pointed out that these might have been slowly growing osteogenic sarcomas present from the first or secondary sarcomas arising at the site of an unhealed lesion in bone.

The differential microscopic diagnosis of giant cell tumor has been discussed, and a short summary of the diagnostic features of osteogenic sarcoma with giant cells included.

A review of the results of various types of treatment in over 200 cases of giant cell tumor has been presented.

# THE EMPTYING OF THE GALLBLADDER FOLLOWING RESTORATION FROM ACUTE EXPERIMENTAL CHOLECYSTITIS \*

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Many investigators in the field of physiology of the gallbladder maintain that the emptying mechanism of the gallbladder is a complex one associated with many interrelated factors. Others, in the light of experimental data, are inclined to emphasize the primary significance of a contractile mechanism within the wall of the gallbladder. Undoubtedly there is a fundamental factor which controls this physiologic process, and yet one which is so closely involved with other secondary factors that an exact evaluation is often difficult. Copher, Kodama and Graham (1926)<sup>1</sup> stated that the dilution and interchange of bile are factors influencing the mechanism by which the gallbladder empties. Other experimental observations have shown that the gallbladder may distend or recoil, reactions which are entirely independent of an active contractile mechanism<sup>2</sup>. It is probably true that the abundant elastic tissue within the wall of the gallbladder increases the effectiveness with which the smooth musculature operates. It has been shown, too, that the passive mechanical emptying of the gallbladder is influenced by the tonicity of the muscle bundles at the ampullar end of the common bile duct. Nevertheless, the preponderance of the experimental observations on the gallbladder, either visualized with iodized oil or by direct observation, shows that changes in the vesicle following the ingestion of a meal rich in fat are due to active intrinsic muscular contraction<sup>3</sup>. Graham and his colleagues maintained that although there are many experimental

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\* Submitted for publication, Dec 10, 1929

1 Copher, G H, Kodama, Shuishi, and Graham, E A. The Filling and Emptying of the Gallbladder, *J Exper Med* **44** 65, 1926

2 Burget, G E. The Regulation of the Flow of the Bile. III. The Role of the Gallbladder, *Am J Physiol* **81** 422, 1927

3 Boyden, E A. The Effect of Natural Foods on the Distention of the Gallbladder, With a Note on the Changes in Pattern of the Mucosa As It Passes from Distention to Collapse, *Anat Record* **30** 330, 1925. Higgins, G M, and Mann, F C. Observations on the Emptying of the Gallbladder, *Am J Physiol* **78** 339, 1926. McMaster, P D, and Elman, Robert. On the Expulsion of the Bile by the Gallbladder and a Reciprocal Relationship with the Sphincter Activity, *J Exper Med* **44** 173, 1926. Whitaker, L R. The Mechanism of the Gallbladder, *Am J Physiol* **78** 411, 1926

data to warrant the assertion that the contraction of an intrinsic musculature does occur the question of primary importance is whether or not these contractions alone are sufficient to empty the vesicle. Graham had previously noted "Shadows of diseased gallbladders were found, by cholecystography, not to change in size when the pathological changes in the wall were moderately advanced. This fact indicated that the fibromuscular layer of the wall had lost its distensibility and power of contractility. Doubtless, too, the malfunctioning of the contractile mechanism prevents normal contraction." With these clinical observations in mind one of us (G. T. M.) undertook an experimental study of the acutely inflamed gallbladder in dogs, noting especially the response following the ingestion of the usual test meal.<sup>4</sup> The conclusions arrived at in his study rather definitely substantiate the hypothesis of a contractile gallbladder, in that the acutely inflamed gallbladder does not empty in the usual way following the fat meal. Histologic evidence shows that in these experimental inflammatory reactions the entire wall of the gallbladder is invariably involved, so that the muscular layer of the vesicle has lost its power to contract. It seems evident, therefore, that the factors causing a normal gallbladder to empty following a fat meal lie within the wall of the vesicle itself and not without. For in these experimental animals, all other factors, such as intra-abdominal pressure, respiratory pressure or secretory activity of the liver frequently credited to the mechanism active in the emptying of gallbladders, are unimpaired.

Since it was evident that the acutely inflamed gallbladder did not empty following the usual test meal, we were interested to know whether the ability to respond to the fat meal had been restored in an animal after restitution from such acute experimental cholecystitis.

#### TECHNIC

Acute pathologic lesions of varying degrees were produced within the walls of the gallbladders of a series of dogs following the intravenous injection of an acid solution of hypochlorite (Lorrain Smith) (eusol) identical with that employed by one of us (G. T. M.) in 1929 in his original study. Eusol is prepared by placing 12.5 Gm. of sodium hypochlorite and 12.5 Gm. of crystalline boric acid in 1 liter of distilled water. The preparation is filtered through filter paper twelve hours later and is then ready for use. Approximately 20 cc. of the solution for each kilogram of body weight was injected into the jugular vein in from one to three injections. The animals were then explored under ether anesthesia with aseptic technic, and the extent of the

<sup>4</sup> Murphy, G. T. The Effect of Acute Experimental Cholecystitis on the Emptying of the Gallbladder. This article will appear in a future issue of the ARCHIVES OF SURGERY.

pathologic lesions was carefully noted and recorded. Figure 1 is typical of the generalized lesion which involves a large part of the fundus of the gallbladder. The fibromuscular layer is especially involved, and the hemorrhage extends also into the elastic and subepithelial regions. The mucosa, however, is usually not involved. From four to six weeks later, under ether anesthesia, a second exploration was made. The gallbladder, which at the earlier laparotomy had shown marked cholecystitis, was now without visible lesions, and it was evident, at least grossly, that

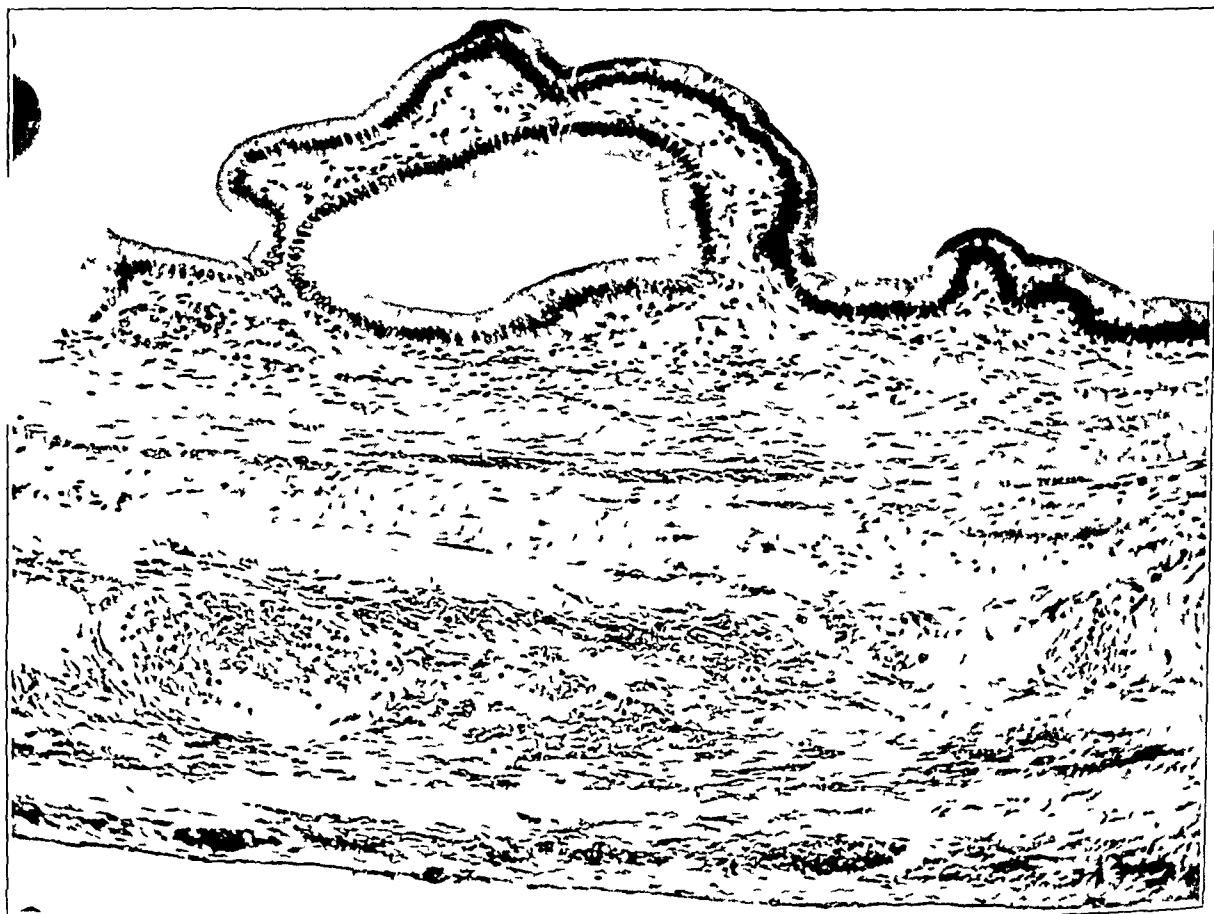


Fig 1—Wall of an acutely inflamed gallbladder, the vesicle did not contract following a meal of egg-yolk and cream, excessive hemorrhage throughout muscle layer is shown ( $\times 125$ )

restoration had taken place. Accordingly, in order to test the emptying of the vesicle, the gallbladder was aspirated through a pursestring suture of blood vessel silk, and an equal amount of iodized oil was introduced into the viscus. From six to eight hours later the animals were given the usual amount of egg-yolk and cream, and roentgen observations were made at frequent intervals thereafter. Six dogs comprised the series of animals which forms the basis of this report.

## RESULTS

Röntgen studies on the emptying of the gallbladder in these experimental animals following restitution from acute cholecystitis did not reveal appreciable differences in the reaction from the behavior of the normal gallbladder following a fat meal. All of the six animals comprising the series which had shown marked cholecystitis at the first laparotomy six weeks before now gave roentgenologic evidence of emptying within thirty minutes after eating (fig 2). The degree of cholecystitis recognized at the first laparotomy did not appear to bear any relationship at this time to the extent to which the gallbladder emptied. In all animals irrespective of the original lesions, the viscus discharged its contents in a normal manner so that the emptying of

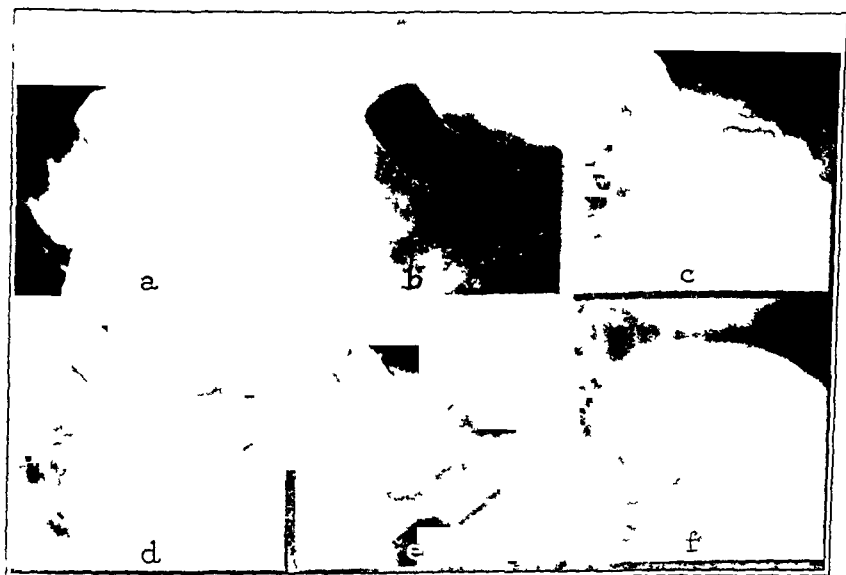


Fig 2—A series of cholecystograms of a gallbladder six weeks after the development of acute experimental cholecystitis *a* before the feeding of egg-yolk and cream *b*, fifteen minutes after feeding *c* thirty minutes after feeding, *d* one hour after feeding *e*, two hours after feeding and *f* three hours after feeding

the gallbladder, after restoration had taken place did not appear to be influenced by the extent of the earlier lesions. Furthermore, if we are to judge by the extent of contraction manifested by the amount of iodized oil in the duodenum and common bile duct there appears to be a close similarity in the functional activity of these gallbladders after restoration of a normal tunc has taken place. Furthermore there does not appear to be any significant difference in the emptying time of the gallbladder between the normal animal and these experimental dogs in which restoration had taken place following acute cholecystitis. Cholecystograms of the normal control animals following a fat meal



are generally similar to those obtained in animals following restoration. Six weeks after the development of the lesions there was no indication in any animal of this series that the function of the emptying mechanism of the gallbladder had been permanently impaired. Furthermore, histologic examination of the wall of the restored gallbladder did not show a residual lesion that could modify in any way the contraction of the

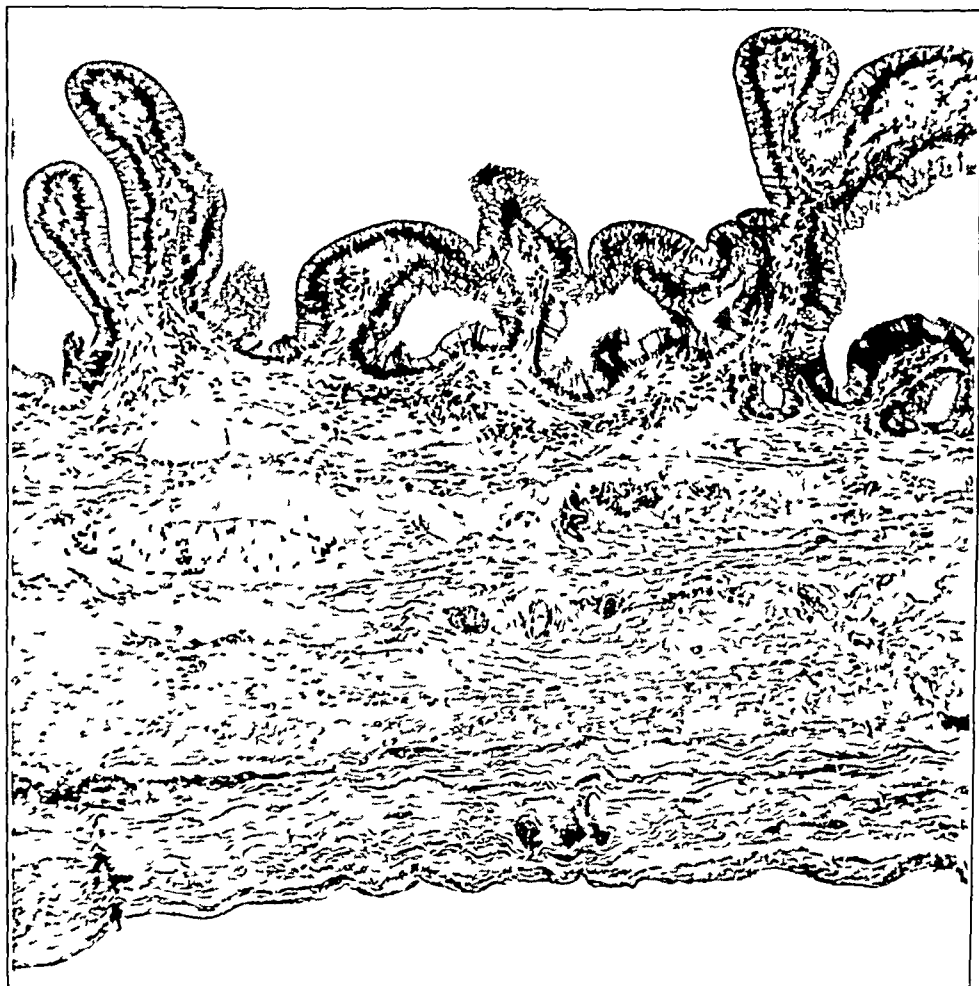


Fig 3—Wall of a restored gallbladder, six weeks after the development of acute cholecystitis, the gallbladder emptied following a meal of egg-yolk and cream ( $\times 100$ )

intrinsic muscle layer. In some sections hemorrhagic exudates were still visible, but they were not extensive and no doubt were without effect on the discharging mechanism (fig 3).

#### COMMENT AND SUMMARY

These experimental observations are of value for several reasons. In the first place, they show the rapidity with which the acutely inflamed

gallbladder may be restored to a functionally normal condition. Within from four to six weeks after the development of acute cholecystitis by the intravenous injection of casein the lesions had practically cleared up and both macroscopically and microscopically a normal condition of the gallbladder was restored. With such restoration there was an accompanying return of functional activity, at least as far as ability to contract and thus to empty following the fat meal is concerned.

Acutely inflamed gallbladders do not empty following the usual test meal. This we believe must be due to a disturbance within the wall of the gallbladder and not to other extraneous physiologic factors. Animals with acute experimental cholecystitis are otherwise, as a rule, in good health. They ordinarily lap their meal of fat and we have no reason to suppose that the normal digestive and assimilative faculties are in any sense disturbed. The injected solution appears to be specific for the gallbladder for we have not identified lesions elsewhere that were induced by the injections. Accordingly, we believe that the inability of the gallbladder to empty is due to the intense inflammatory reaction which ordinarily involves the entire wall of the gallbladder, including the muscularis layer, thus inhibiting its power to contract.

When these gallbladders have been restored to a healthy condition and the inflammatory reaction has cleared up, a discharge of bile from the gallbladder invariably follows the ingestion of the fat meal. Normal, functional tissue has apparently been restored, an intact muscular layer is reestablished, and the vesicle may again respond to the factors, whether of a hormone-like nature or not, which incite the vesicle to discharge its contents.

These studies, therefore, seem to substantiate our earlier observations, and those of other workers, in the field of physiology of the gallbladder, that the primary mechanism causing the discharge of bile from the gallbladder lies within the vesicle itself. In experimental animals with acute cholecystitis, so far as we are able to determine all other conditions are normal. Peristalsis goes on, the flow of bile remains undisturbed and we have no reason to believe that the sphincteric mechanism at the duodenal end of the common bile duct is under unusual tonus, inhibiting the flow of bile from the gallbladder. Certainly, abdominal or respiratory pressure does not differ in these animals, and thus we believe that the structural mechanism within the wall of the gallbladder, known to be seriously impaired in these experimental animals, is the factor largely responsible for the inhibitory action in cholecystitis. Accordingly, in the light of these experimental observations on both normal and abnormal gallbladders in dogs the normal gallbladder undoubtedly empties by a contractile mechanism within the wall of the vesicle, and the diseased gallbladders do not empty because this contractile mechanism has become seriously impaired making its usual response to the inciting stimulus impossible.

# GOITROUS ENLARGEMENT OF THE THYROID GLAND DUE TO AMYLOIDOSIS \*

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In generalized amyloidosis, deposits are not uncommonly found in the vessels of the thyroid as well as in other organs, but the quantity is rarely sufficient to produce enlargement of the gland or in any other way to give evidence of its presence during life. Little mention is made in the literature of amyloid goiter or localized amyloidosis of the thyroid without demonstrable deposits elsewhere. The rarity of the condition together with its interesting clinical and pathologic manifestations warrant the recording of further instances.

## REPORT OF A CASE

*History*—Mr H N, aged 54, entered St Vincent's Hospital on the service of Dr T M Joyce on March 3, 1929. The patient had noticed an enlargement of his thyroid gland for two years before admission, but no symptoms had developed until the last three months. At the time of entry, these consisted of dysphagia, dyspnea on exertion and an uncomfortable sensation of pressure in the neck. He said that he had not had a cough, fever and night sweats or any other complaint, which was surprising in view of the physical observations.

*Examination*—Examination revealed a small asthenic person, with a blood pressure of 150 systolic and 90 diastolic, a temperature of 99.2 F, and a pulse rate of 84 beats per minute. He had a definitely enlarged thyroid gland, which was rather soft and somewhat irregular. The physical signs of a moderately advanced tuberculosis in both upper lobes were present and were substantiated by roentgenologic studies and examination of the sputum. His basal metabolic rate was within normal limits. The remainder of the examination gave negative results, with the exception of a secondary anemia, hemoglobin, 65 per cent, erythrocytes, 4,250,000, and leukocytes, 9,000. The Wassermann reaction was negative.

*Operation and Course*—Operation was advised in spite of the active tuberculosis, because the pressure on the trachea was becoming intolerable. On March 4, 1929, a bilateral partial lobectomy was performed, and the isthmus was divided to insure relief from tracheal pressure. The gland was quite large and of most unusual appearance. It was yellowish white, of the consistency of soft butter, and was practically avascular.

The postoperative course was uneventful. The patient changed his habits as far as he was able, in order to increase his resistance to the tuberculous infection. He appeared to be getting along well in November, 1929.

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It was evident from the peculiar appearance and the absence of vascularity that we were dealing with a gland in which some unusual process was taking place and this was borne out by the pathologic studies.

Three months following thyroidectomy the patient was given intravenously 0.15 Gm of Grubler's congo red dye. Colorimetric examination of the plasma withdrawn from the vein of the arm one hour after injection showed an absorption of only 22 per cent of the dye. This indicated an absence of appreciable amounts of amyloid in organs other than the thyroid gland since 60 per cent or more of the dye must disappear from the blood stream before the test can be regarded as clinically significant of amyloidosis.

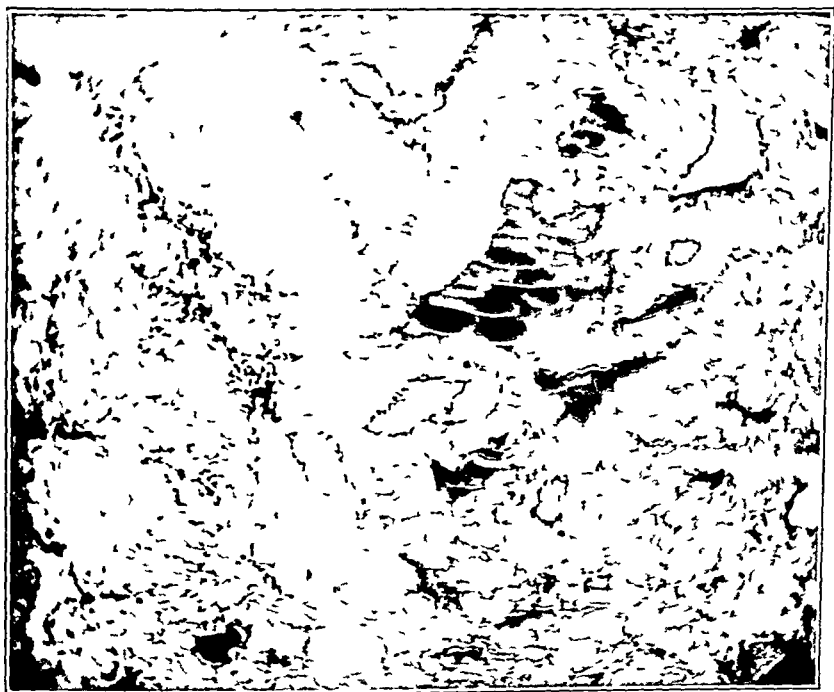


Fig 1—Low power photomicrograph of thyroid gland which was stained with hematoxylin and eosin. Notice the great reduction in the number of alveoli with marked distortion and the extensive and diffuse amyloid infiltration.

*Pathologic Study*—Gross Examination. The specimen consisting of the greater part of each lateral lobe of the thyroid weighed 248 Gm. The lobes measured 3.5 by 7 by 11 cm and 3 by 4 by 11 cm respectively. Externally, both were smooth, regular in outline and covered by a thin fibrous capsule. The parenchyma cut with unusual ease, and the surfaces so made were diffusely yellowish brown, soft and looked not unlike fat. Colloid was scanty, with only occasional pinpoint to pinhead sized glassy colloid-containing areas scattered here and there throughout the gland. The trabeculae were not widened and no nodules were observed. The gross test for amyloid, made by placing portions of the gland in compound solution of iodine followed by placing them in dilute sulphuric acid gave a strongly positive reaction.

**Microscopic Examination** Sections from various parts of the gland revealed a most striking alteration in its structure. The acini were greatly reduced in number. Those that remained, while usually fairly large and filled with colloid, were almost without exception flattened, elongated or even stellate-shaped. The colloid was vacuolated, and embedded in it were degenerating desquamated epithelial cells. In most of the acini the cells were flattened or cuboidal, but they occasionally showed slight papillary infolding. The most outstanding change, however, was the enormous amount of homogeneous hyaline-like substance which everywhere lay between and widely separated the alveoli from each other. Buried in this substance were clumps of cells which appeared to be the flattened atrophic remains of alveoli. Mixed with the homogeneous material were groups of oval or

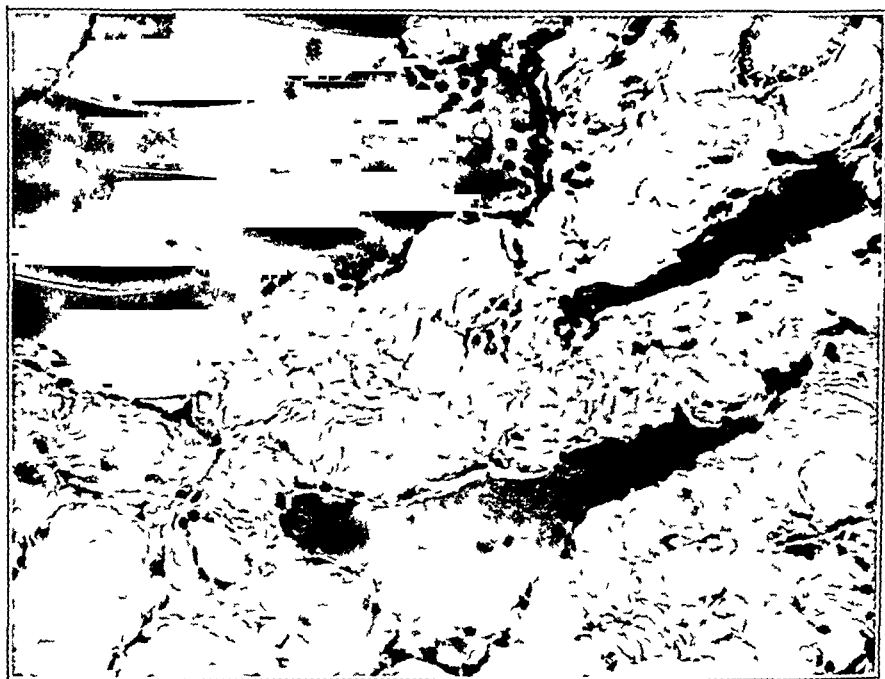


Fig 2—High power microphotograph of a part of the same field shown in figure 1. The alveoli are compressed and irregular due to the abundant amyloid substance laid down between and around them. Note also the flattened atrophic acinar epithelium.

rounded vacuolar spaces having the histologic structure of fat cells. In a number of sections there were small areas of active fibroblastic proliferation, lymphoid cell collections, and what seemed to be either degenerating remnants of acinar cells or pseudo-giant cells. Such foci occurring in tissue from a tuberculous subject suggested the possibility of tuberculosis, but the absence of epithelioid cells and caseation necrosis together with the well recognized fact that closely grouped degenerating alveolar cells may resemble giant cells made this unlikely. In methyl-violet preparations, the hyaline-like substance stained a deep red, thereby proving the presence of an extensive amyloid infiltration. With this stain it was found that the amyloid completely filled most of the interalveolar vascular spaces and obliterated all save the larger vessels, and these too showed a moderate sub-endothelial amyloid infiltration.

**Pathologic Diagnosis.** The pathologic diagnosis was marked diffuse amyloidosis of the thyroid gland with atrophy and degeneration of the thyroid parenchyma (amyloid goiter).

## COMMENT

The real or apparent rarity of amyloid goiter is shown by the paucity of reports in the literature. Prior to 1857, only fifteen instances<sup>1</sup> were on record. Peters<sup>2</sup> could find only ten authentic cases up to 1898, to which he added eleven of his own. In thirteen of the fifteen instances mentioned by Stoffel there was a generalized amyloidosis occurring in the presence of such diseases as tuberculosis, syphilis or a malignant disease to explain the amyloid formation. Amyloid was present in other organs as well as in the thyroid gland in all of Peters' cases. The apparent rarity of amyloidosis of the thyroid gland may be due to a failure of workers to record their observations. Osgood<sup>3</sup> saw two cases among 400 selected autopsies in Erdheim's service. On the other hand the case reported herein was the first encountered in approximately 3 500 operations on the thyroid gland in the clinic of Dr. T. M. Joyce.

Von Eiselsberg's<sup>4</sup> account of a syphilitic man who, because of a history of rapid enlargement of the thyroid gland came to operation with the clinical diagnosis of a probable malignant condition is of unusual interest. While removing the supposedly malignant gland, von Eiselsberg noted a striking lack of bleeding although the patient's circulation was good. The ligatures about the vessels of the gland cut through, but still hemorrhage did not occur and the man made an uneventful recovery except for symptoms that may be interpreted as parathyroid tetany. The goiter was remarkably brittle, bacon-like and pale yellowish. Sections stained with gentian violet gave a definite amyloid reaction. The acini were sparse, with an abundance of amyloid between them. The blood vessels, which could be found only after long search, contained no blood and showed "colloid" degeneration of their walls. The obliteration of the vascular apparatus adequately explained the lack of bleeding encountered during the operation. Von Eiselsberg could find no other instances of amyloidosis which had produced compression of the trachea. Stoffel's patient with coexistent carcinoma and amyloidosis of the thyroid gland experienced respiratory difficulty from pressure stenosis of the trachea. Stoffel stated that most of the amyloid lay in the interstitial tissue and that little was present in the blood vessel walls.

1 Stoffel, Edda. Lokales Amyloid der Schilddrüse, *Virchows Arch f path Anat* **201** 245, 1910.

2 Peters, W. Ueber einem Amyloid-Tumor mit Metastasen, *Inaug Dissertation*, Tübingen, 1901.

3 Osgood, E. E. *Personal communication to the author*.

4 Von Eiselsberg, F. Ueber einem Fall von Amyloid-Kropf, *Arch f klin Chir* **73** 649, 1904.

More recently, Ipland<sup>5</sup> recorded three instances of generalized amyloidosis in tuberculous subjects showing marked infiltration of adenomas of the thyroid gland while the remainder of the gland was comparatively free. Observations of amyloid depositions in adenomas of the thyroid gland appeared to be even more rare than those of diffuse amyloidosis.

#### SUMMARY

1 An instance of advanced amyloidosis of the thyroid gland producing enlargement of the gland and symptoms of pressure stenosis of the trachea is reported.

2 Chronic pulmonary tuberculosis, the most common cause of amyloid formation, adequately explains its presence in this case.

3 The results of the congo red absorption test indicate that the patient did not have a widespread amyloidosis.

4 The present study confirms the observation of previous investigators that in the thyroid gland amyloid substance is deposited chiefly in the vascular interalveolar spaces.

5 Amyloidosis of the thyroid gland is seldom encountered in surgical practice. The nature of the process may be suspected or diagnosed at operation by the bacon-like or fatty appearance of the gland and distinguished from a malignant process by the almost complete lack of hemorrhage during the course of the operation.

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<sup>5</sup> Ipland, H. Ueber Amyloid in Adenomen der Schilddrüse, Frankfurt Ztschr. f. Path. **16** 441, 1915.

# TREATMENT OF BRONCHIECTASIS—MULTIPLE STAGE IODOLIOLOGY

REPORT OF TWO CASES \*

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The extensive use of iodized oil according to the method introduced by Sicard and Forestier,<sup>1</sup> in the roentgenographic investigation of chronic pulmonary suppurations has shown an unsuspected frequency of bronchiectasis. It has brought about a separation of this disease from tuberculosis, chronic empyema with bronchial fistula, chronic bronchitis and even from some forms of asthma, but, on the other hand, it has also shown how often these conditions are associated with bronchial dilatations.

The most important contribution of this method of investigation has been that it has permitted tracing the disease from its earliest forms, when clinical symptoms and simple roentgenograms give no information whatever, and has established the fact of the great frequency of the disease in childhood following measles, scarlet fever and especially chronic inflammation of the paranasal sinuses. Sauerbruch<sup>2</sup> has even maintained that a great number of bronchiectases are due to congenital cystic dilatations of the bronchial tree.

It has thus come to be recognized that bronchiectasis is a common pulmonary disease. Hedblom<sup>3</sup> considered it as frequent as tuberculosis, Hamilton<sup>4</sup> stated that from 25 to 50 per cent of the patients

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1 Sicard, J. A., and Forestier, J. *Methode generale d'exploration radiologique par l'huile iodee (Ipiodol)*, Bull. et mem. Soc. med. d. hop. de Paris **46** 463, 1922, *exploration radiologique par l'huile iodee*, Presse med. **44** 493 (June) 1923, *Diagnostic et therapeutique par le Ipiodol*, Paris, Masson & Cie, 1928 (in this volume a complete bibliography is given).

2 Sauerbruch, F. *Die chirurgische Behandlung der Bronchiektasien*, Wien klin. Wchnschr. **40** 543 (April 21) 1927.

3 Hedblom, C. A., and Head, J. R. *The Diagnosis and Treatment of Bronchiectasis*, J. A. M. A. **89** 1384 (Oct. 22) 1927.

4 Hamilton, W. F. *Nontuberculous Pulmonary Disease*, Arch. Surg. **14** 218 (Jan.) 1927.



sent to sanatoriums for tuberculosis have bronchiectasis, and Ochsner<sup>5</sup> found that 95 per cent of patients with chronic bronchitis with persistent cough show bronchial dilatation in roentgenograms taken following the injection of iodized oil

Twenty per cent of all cases of chronic tuberculosis (Landis) and 10 per cent of cases of tumor of the bronchi or lungs, foreign bodies (Jackson<sup>6</sup>) or extrinsic compressions of the bronchi are complicated by bronchiectasis. This shows not only the great frequency of the disease, but also the variability of its clinical forms. As Brunn and Faulkner<sup>7</sup> stated, the term "bronchiectasis" must no more bring to mind the picture "of a hopeless patient with pasty septic look, harassing cough, clubbed fingers and copious foul expectoration and one whose obnoxious breath practically ostracizes him from human association." Bronchiectasis "is a very chronic disease, beginning frequently in early childhood, with symptoms of only moderate severity, extending over several years and perhaps never reaching the ultimate stages classically ascribed to it."

#### CLINICAL FORMS OF BRONCHIECTASIS

From the foregoing consideration it is obvious that the treatment of bronchiectasis may be a variable proposition because of the wide variety in the evolutionary phases and clinical forms of the disease. It is therefore indispensable for a clearer conception of the treatment to distinguish in bronchiectasis a number of clinical varieties, as follows:

1 Bronchitic form (Ochsner<sup>5</sup>) in which none of the classic symptoms of bronchiectasis is present, the bronchial lesions are slight and the parenchyma of the lung is healthy. Only roentgenograms taken following the injection of iodized oil reveal the disease.

2 Early uncomplicated bronchiectasis (Hedblom<sup>8</sup>) in which bronchial lesions are definitely present, but are still limited to the bronchi. No pneumonitis is found in plain roentgenograms. In the roentgenograms of the bronchi there are seen cylindric or saccular dilations of the bronchi, clubbing of the fingers is present, but there is no foul sputum, or fever or loss of weight. The lesion is generally unilateral or at least more accentuated in one lung and more particularly in one lobe.

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5 Ochsner, Alton. An Unappreciated Cause of Chronic Bronchitis, *J A M A* **93** 188 (July 20) 1929.

6 Jackson, C. Chronic Nonspecific Infections of the Lungs—Their Bronchoscopic and Esophageal Phases, *J A M A* **87** 729 (Sept 4) 1926.

7 Brunn, H., and Faulkner, W. B., Jr. Bronchiectasis, *Am Rev Tuberc* **19** 191, 1921.

8 Hedblom, C. A. Uncomplicated Unilateral Bronchiectasis. Late Results of Extrapleural Thoracoplasty, *Arch Surg* **14** 389 (Jan) 1927.

3 Complicated bronchiectasis with more or less advanced pneumonitis or even small multiple bronchiectatic abscesses, corresponding to the classic form of bronchiectasis (foul sputum, persistent cough, a more or less septic appearance, intermittent fever, loss of weight and markedly clubbed fingers are present)

4 Bronchiectatic abscesses, found unilobar, unilateral or diffuse according to the distribution of the disease

Besides these forms, which depend on the pathology of the disease, one must distinguish clinical forms according to the age of the patient and according to the evolution of the lesions

Guibal<sup>9</sup> in an excellent monograph on the subject, described as found in the young, besides the congenital forms already spoken of other clinical types

1 Acute bronchiectasis, which may appear in the course of whooping cough or measles and disappear without leaving any sequelae

2 Latent bronchiectasis, chronic in its evolution and only revealed by acute exacerbations

3 Chronic bronchiectasis, which should be likened to the chronic form of adults, and which responds to surgical treatment

In the adult, two forms are observed

1 Latent bronchiectasis with acute episodes, which is compatible for a long time with good general health

2 The chronic form

Guibal raised an important question when he asked whether there are an acute and a subacute bronchiectasis. Oftentimes, cases have been reported in which, after an acute pulmonary disease, pneumonia or bronchopneumonia, abundant expectoration and signs of small cavitation, verified by operation, have developed (Kammerer<sup>10</sup> Frankel and Korte,<sup>11</sup> Delbet<sup>12</sup> and others). These lesions generally heal rapidly after pneumonotomy or collapse therapy (Roux-Berger, Guibal). Aschner<sup>13</sup> believed, and Guibal concurred in the opinion, that in these cases there is a "suppurative pneumonitis" with small abscesses developed in the parenchyma of the lung and not real bronchiectatic lesions. There is

9 Guibal, M. L. Sur le traitement chirurgicale de la dilatation bronchique chronique quatre observations personnelles, Paris Masson & Cie, 1924. Bull et mem Soc nat de chir **1** 312, 1924.

10 Kammerer, F. Operation for Bronchiectasis. Ann Surg **49** 865, 1909.

11 Fränkel, A. and Korte, W. Gegenwartiger stand d Lungenchirurgie. Verhandl d Berl med Gesellsch **43** 25 1912.

12 Delbet, P. Sur les décollements pleuropulmonaires. Bull et mem Soc nat de chir **47** 400 1921.

13 Aschner, P. W. The Pathology of Lung Suppuration. Ann Surg **1** 321 1912.

no doubt that clinical observation shows a close relationship between pathologic conditions of the upper and lower parts of the respiratory tract. Acute coryza, sinusitis and tonsillitis are often accompanied by pulmonary signs or even the flaring up of old pulmonary lesions, although the intermediate section of the respiratory tract presents no change. The fact has been stressed by A. Miller of New York, in his teaching, that in old foci of tuberculosis evidenced by only a few dry râles an acute condition may develop under the influence of acute coryza or sinusitis, but that it will readily clear up following the healing of these inflammatory lesions of the upper part of the respiratory tract. In the same way, bronchiectasis in its early stages is greatly improved or even heals following treatment for sinusitis and tonsillitis and a sojourn in a dry, hot climate. I venture a suggestion that acute bronchiectasis might be due to acute lymphangitis of the bronchopulmonary and intrapulmonary lymphatic system, lymph nodes and lymph cells aggregates. Both, as is known, are located in the angles of division of the extrapulmonary and intrapulmonary bronchial tree, down to the divisions of the respiratory bronchioles and alveolar ductules. As Lerche<sup>14</sup> pointed out, it seems probable that their enlargement might, by a compression of the respiratory tubes, produce narrowing of their diameter and impairment of their free drainage. Incomplete bronchial obstruction and bronchial stasis would lead to signs of acute bronchiectasis, which would subside with clearing up of the initial infection and the subsequent decrease in size of the lymph nodes. It is easily understood how repeated infections of the upper part of the respiratory tract may lead to chronic adenopathy, and furthermore to a spreading of the infection from the lymphatics to the musculo-elastic element of the bronchioles, thus leading to their permanent enlargement and chronic inflammatory changes of the surrounding parenchyma. This hypothesis on which experimental investigation is now actually being carried on could give the key to the progressive nature of bronchiectasis and to its different clinical forms.

#### OUTLINE OF TREATMENT

The distinctions in form that have been mentioned are certainly schematic, for bronchiectasis is a progressive disease which, if left alone, tends gradually to pass from one form to the other in the great majority of cases.

It is not the aim of this paper to discuss the general treatment of bronchiectasis. I shall remark only that in the bronchitic form a careful examination and treatment of the paranasal sinuses associated with

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<sup>14</sup> Lerche, W. Infections of the Lymphnodes of the Bronchial Tree, *Arch Surg* 16 338 (Jan) 1928.

hygienic measures, a hot dry climate and postural and bronchoscopic drainage will in a number of cases check the progress of the disease

In the second form, the early uncomplicated bronchiectasis, besides these measures, a therapeutic compression of the lung should be considered, the parenchyma of the lung is still compressible and collapsible. Pneumothorax, phrenicectomy or even thoracoplasty associated with postural and bronchoscopic drainage of the bronchi and anti-spirochetal treatment, when necessary, have given many satisfactory results (Hedblom<sup>8</sup>). It is obvious that these suggestions apply especially to cases of unilateral bronchiectasis. I do not say exclusively because it has been shown that in cases of bilateral bronchiectasis in which there is a clearcut predominance on one side, the less affected side is greatly improved by treatment of the more affected side (see case 1).

In the third, or advanced, form of bronchiectasis with pneumonitis and multiple bronchiectatic abscesses, if the general condition of the patient allows, there is but one curative treatment, and this is the surgical exeresis of the diseased portion of the lung by lobectomy (Sauerbruch,<sup>2</sup> Lilienthal<sup>15</sup> Robinson,<sup>16</sup> Brunn<sup>17</sup> and others), cautery pneumectomy (Graham<sup>18</sup>) or exteriorization and ligation of the involved parenchyma of the lung (Zaaijer,<sup>19</sup> Whittemore<sup>20</sup> and others).

I wish to emphasize the point that bronchiectasis is a chronic and slowly progressive disease and is amenable to progressive treatment. Moreover, clinical and experimental work has convinced me that the treatment in stages as outlined, should be applied as well to advanced cases of bronchiectasis, thus preparing the ground for the terminal stage, or surgical exeresis of the diseased lung. I am convinced that by this progressive treatment not only will indications of lobectomy become less frequent but what is more, the present prohibitive mortality following this operation will be markedly decreased. One should keep in mind that in the progressive forms procrastination is perhaps a more

15 Lilienthal, H. Pulmonary Abscesses and Bronchiectasis, *Ann Surg* **59** 855, 1914. Resection of the Lung for Suppurative Infections with a Report Based on Thirty-One Operative Cases. *Ann Surg* **75** 257, 1922.

16 Robinson, S. The Surgery of Bronchiectasis Including a Report of Five Complete Restorations, *J Gynec & Obst* **24** 194, 1917, The Resection of Lobes of the Lung, *J A M A* **69** 355 (Aug 4) 1917.

17 Brunn, H. Surgical Principles Underlying One Stage Lobectomy, *Arch Surg* **180** 490 (Jan) 1929.

18 Graham, E. A. Cautery Pneumectomy for Chronic Suppuration of the Lung. A Report of Twenty Cases, *Arch Surg* **10** 392 (Jan) 1925.

19 Zaaijer, I. H. Zur Therapie der Bronchiektasen. *Deutsche Zt-schr f Chir* **200** 17, 1927. Surgery of the Oesophagus and Lungs. *Lancet* **1** 909, 1929.

20 Whittemore, W. The Treatment of Chronic Suppurative Bronchiectasis. *Ann Surg* **86** 219, 1927.

dangerous procedure than radical surgery, that, if one is obliged to operate, this is better done while the general condition of the patient is still good, while the myocardium, the liver and the kidneys are still in good condition, and before there develop too many pleuropulmonary adhesions which may offer insurmountable technical difficulties for operation. If I am tempted to advise greater boldness for the internist, I should urge the thoracic surgeon to conservatism. I do not mean by conservatism that one should refrain from operating. On the contrary, one should and one certainly will operate in the future much more than one does now. I mean that one must not forget that thoracic surgery is the only branch of surgery in which the mere approach to the organs concerned involves an immediate and dangerous disturbance of the functions of respiration and circulation. For this reason, one should become more acquainted through experimental and clinical investigation, with the normal and pathologic physiology of these functions, as yet so incompletely known. Moreover, one should sacrifice the brilliancy of one-stage operations for the greater safety of graded ones, above all, one should adjust one's operative procedures to the resistance of the patient, preferably doing much less each time than a little more than what the patient can withstand. In other words, I am a firm believer in graded operations, which, especially in bronchiectasis, have the great advantage of gradually improving the condition of the patient, as will be shown in the remarks to follow.

*Graded Lobectomy*—By graded lobectomy is meant the technic by which the patient is purposely prepared for the exeresis of the diseased lung, by systematic use, in the order given, of pneumothorax, phrenicotomy, graded thoracoplasty and, in some cases, ligation of the corresponding branch of the pulmonary artery. Several authors have reported cases in which lobectomy was performed after thoracoplasty because the latter procedure did not cure the disease, but it has not been carried out, to my knowledge, purposely as a preliminary measure to lobectomy. Sauerbruch<sup>21</sup> reported six cases in which lobectomies performed after ligation of the pulmonary arterial branch did not cure the disease. None of these patients died, all had bronchial fistula, five were clinically cured and one improved. It is interesting to note that the same author<sup>22</sup> reported four cases of lobectomy in one stage, with four deaths. Hedblom<sup>23</sup> advocated graded thoracoplasty in the treat-

21 Sauerbruch, F. *Chirurgie der Brustorgane*, ed 2, Berlin, Julius Springer, 1920.

22 Sauerbruch (footnote 21, vol 1, p 588).

23 Hedblom, C. A. Graded Thoracoplasty for Unilateral Bronchiectasis, *Wisconsin M. J.* 21 48 (July) 1922, Graded Extrapleural Thoracoplasty in the Treatment of Diffuse Unilateral Bronchiectasis, *Arch. Surg.* 8 394 (Jan) 1924, footnotes 3 and 8. Hedblom, C. A., and Head, J. R. Use of Lipiodol in Relation to Thoracic Surgery, *Ann. Surg.* 85 194 (Feb) 1927.

ment of bronchiectasis. In three of these cases, in which the condition was relieved but not cured, he performed a secondary lobectomy in two stages. In one definite cure followed, in the other, the patient died a week after operation, and in the third the patient died during operation while traction was being exerted on the pedicle of the lung. Krause, Heidenhain, Archibald<sup>24</sup> and de Quervain reported similar cases, with a successful outcome. Hedblom<sup>2</sup> concluded "Primary lobectomy and cautery extirpation are not to be recommended on account of the high post-operative mortality and the frequency of residual bronchial fistula. Secondary lobectomy or graded cautery extirpation, when indicated, following thoracoplasty and phrenico-exeresis should prove relatively safe and highly effective." Zaaijer<sup>19</sup> is the only author who advocated as successive stages phrenicectomy, thoracoplasty, thoracotomy and liberation of the diseased lung from adhesions, followed by packing, and as the last stage, resection of the involved lobe by elastic ligation of the bronchus. He remarked that "each of this series of operations may result in a clinical cure and each prepares for the following one and renders it less dangerous."

Against the views of these authors, one finds Sauerbruch<sup>2</sup>, Lilienthal,<sup>25</sup> Tuffier, Batzdorf, Garre, Robinson<sup>16</sup> and more recently Brunn<sup>17</sup> (with six lobectomies followed by five postoperative recoveries), who with more or less reservation are in favor of one-stage lobectomy. Whittemore<sup>20</sup> used to operate in one stage, but because of the high mortality (five of six operations resulting in deaths) abandoned one-stage operation and instead of resecting the involved lobe, now exteriorizes it and fixes the pedicle to the wall after resection of three ribs and allows it to slough away. He has had four postoperative recoveries in five cases in which this operation was done.

Although a few of the authors mentioned have obtained with one-stage lobectomy encouraging results in a limited number of cases, it is certain that the total mortality of one-stage lobectomy is still about 55 per cent, as is shown in the accompanying table.

Sauerbruch<sup>26</sup> found in the literature to 1911, 123 reports of "pneumotomies" with a total mortality of 25 per cent, cures, 33 per cent improvements, 6 per cent, and no improvements, 27 per cent. His personal statistics<sup>21</sup> to 1920 give a mortality of 44.4 per cent. This shows that there is no improvement in the results of lobectomy, and although these results are still encouraging in view of the severity of the disease according to Lilienthal, one should admit that they explain

24 Archibald, E., and Brown, A. L. Danger of Introducing Iodized Oil into the Tracheo-Bronchial System. *J. A. M. A.* 88:1310 (April 23) 1927.

25 Lilienthal, H. Statistics in discussion of Hedblom (footnote 3 p. 1390).

26 Sauerbruch (footnote 31 vol. 1, p. 585).

the hesitation of the internist and the surgeon in advising this operation and carrying it out, particularly in cases of little advanced bronchiectasis

If one compares with these figures the results in lobectomies performed in several stages, one finds Sauerbruch's five cases with no deaths, Guibal's one with no death, and Coryllos' two with no deaths. If one compares the results in cautery pneumectomy, one finds Graham's forty-five cases, with freedom from symptoms after three years in 69 per cent, improvement in 7 per cent and deaths in 24 per cent, Whittemore's six cases with one death, and Hedblom's three cases with two deaths. Considering these figures, one must concede that something is wrong with the technic of one-stage lobectomy.

It will be interesting to discuss the causes of the deaths following lobectomies and study the "pathologic physiology" of this operation, if I may use this term, and see if there is any possibility of improving the results thus far given by it.

*Results of One-Stage Lobectomy in Cases of Bronchiectasis*

Operators				Year	Opera- tions	Cures	Improve- ments	Deaths
Meyer	Tr	Am	S A 32	592, 1914, Arch	1914	16	8	8
Surg	5	361	(June)	1923	1915	1	1	
Robinson	16				1917	7	4	3
Hansen	Nord	med	Ark	1 1 1917	1917	4	3	1
Hitzrot	Ann	Surg	71	785, 1929	1920	1	1	
Sauerbruch	31				1920	3		3
Graham	Arch	Surg	3	21 (Jan) 1923	1923	3	2	1
Guibal	9				1924	6	1	5
Whittemore	20				1927	31	7	24
Lilienthal	25				1927	3	2	1
Whittemore	20				1927	6	5	1
Brunn	17				1929	6	4	1
Mortality = 55.1 per cent					87	38	1	48

THE "PATHOLOGIC PHYSIOLOGY" OF LOBECTOMY AND THE CAUSES OF DEATH

Death during or shortly after lobectomy can be ascribed to (1) shock, cardiac failure (mechanical or reflex) or pleural shock, (2) embolism (air or septic), (3) hemorrhage during and after operation, (4) increased intrapleural pressure during the first days following operation, by pneumothorax or intrapleural fluid, (5) septic pleurisy and (6) septic mediastinitis.

*Shock*—Under the general term of shock in lobectomies, one should consider inhibitory phenomena of different nature and origin, all of which lead to the arrest of cardiac function. Most often they are purely mechanical. The heart in bronchiectasis, with putrid bronchial exudate stagnating in the bronchi, generally presents a more or less advanced toxic myocarditis. Proof of this is given by the tachycardia of the patients. When the chest is opened, especially when there are no marked pleuropulmonary adhesions (as is often the case), a collapse of

the corresponding lung occurs and with the suppression of the ventilation, suppression of the pulmonary circulation results. Thus, the back pressure into the right side of the heart increases and an extra burden is thrown on the heart. Often the heart is able to withstand this extra work, but it is impossible to determine in advance how long its resistance will last. Another factor, equally impossible to gauge in advance which increases the cardiac strain, is the mobility of the mediastinum. Meyer<sup>27</sup> said that 50 per cent of persons have a steady mediastinum, and one thoracic cavity can be opened without disturbing the respiratory function of the other cavity. Unfortunately, one does not know in advance who these fortunate 50 per cent are. A mobile and fluttering mediastinum, after the opening of one thoracic cavity, causes an encroachment on the ventilation and circulation of the healthy lung, which is already hampered by the position of the patient lying on the healthy side of the chest.

As Eloesser<sup>28</sup> remarked in his paper on preliminary artificial pneumothorax, the danger is not only in the sudden collapse of the lung. When one uses positive pressure and artificially expands the lung or, especially, if the patient coughs during operation, "sudden inflation and sudden collapse produce sudden variations in the volume of blood that is thrown into and sucked out of the heart and both are equally terrifying in their effect" on the cardiac function. This "suddenness" is a dangerous element in operations in an open chest.

Besides the mechanical effect on the heart of the variations in the size of the lungs, there is a nervous effect. Through the vagi there is an interrelation between the movements of the lungs and the cardiac function. Moreover, some inexplicable deaths with sudden arrest of the heart after even slight traction on, or manipulation of, the pulmonary pedicle, may be due to an inhibitory cardiac reflex transmitted through the vagi. Sauerbruch,<sup>29</sup> Hedblom (1927)<sup>23</sup> and Eloesser,<sup>30</sup> each reported one death due to such a cause.

*Embolism*—Cough during operation is another cause of death often ascribed to shock. During the gasping inspiration preceding and following paroxysmal cough, the mouths of pulmonary vessels are opened, and air and infectious material are easily forced into them under great pressure. Moreover, as Eloesser rightly remarked, the paroxysms of coughing aspirate and insufflate exudate and septic material from one part of the lung to another and may obstruct a big bronchus of the

27 Meyer, Willy. On Bronchiectasis. *Tr. Am. S. A.* **32** 592 1914. Observations on Lung Suppuration and Its Treatment, *Arch. Surg.* **5** 361 (June) 1923.

28 Eloesser, L. Preliminary Artificial Pneumothorax in Operations on the Open Chest, *Arch. Surg.* **14** 439 (Jan) 1927.

29 Sauerbruch (footnote 21 vol 1 p 588).

30 Eloesser (footnote 28 p 443).



healthy lung (as in the cases of Berry<sup>31</sup>) and cause immediate death by bronchial reflex or obstructive atelectasis or delayed death by infection of the healthy lung

Embolism may be connected with the much discussed "pleural reflex" or pulmonary reflex or pleural eclampsia. Lilienthal<sup>32</sup> did not admit the existence of the latter, considering that in the cases reported the real cause was an embolism. Hedblom,<sup>33</sup> on the other hand, reported a case in which he had purposed to perform a second stage extrapleural thoracoplasty for bronchiectasis. He had just opened the old incision without touching the lung when suddenly the patient went into convulsions, the pupils dilated and the patient became intensely cyanotic but gradually revived. I have seen two similar attacks. The first occurred during a thoracoplasty, second stage, preliminary to a proposed resection of a cancerous esophagus, which was done with the patient under spinal anesthesia. There were sudden convulsions, a comatose condition, dilated pupils and cyanosis. The patient died forty-eight hours later. At autopsy, no air or other embolism or hemorrhage was found in the brain. The second attack occurred in a young woman with an abscess of the right lower lobe. Thoracotomy and a first stage cautery pneumectomy had been performed eight days previously with the patient under infiltration anesthesia, without the slightest trouble. At the second stage, just after the packing was taken off, she had an attack of generalized convulsions, rapid pulse, slight cyanosis, dilated pupils and coma. This lasted five minutes and was followed by a second one, fifteen minutes later, of the same duration. The loss of consciousness lasted about two hours, she came out of the coma gradually and completely. She had never had any attack like this previously, nor were there any thereafter. Was this a mere coincidence? At the time, I thought of a hysterical paroxysm, but my other case and the case mentioned by Hedblom<sup>33</sup> made me think that here is a condition that is not yet understood. Eloesser reported a case in which a sudden arrest of the heart followed clamping of a bleeding branch of the pulmonary artery near the hilum. In that case, an extreme dilatation of the right side of the heart was found. This reminds me of what sometimes happens in experimental work in the chest of the dog. Often the heart allows brisk manipulation, such as the introduction of an instrument through the left auricle or ventricle, without any disturbance of its function. At other times, with the same kind of artificial respiration, the same anesthetic (iso-amyl-ethyl barbituric acid) and the same

31 Berry, F. B. Massive Atelectasis Complicating Paravertebral Thoracoplasty for Pulmonary Tuberculosis, *Arch Surg* **18** 257 (Jan) 1929

32 Lilienthal, H., in discussion of Eloesser (footnote 28), *Arch Surg* **14** 446 (Jan) 1927

33 Hedblom C. A., in discussion of Eloesser (footnote 28, p 446)

technic, without any apparent reason the heart goes into fibrillation and stops, with the right side of the heart extremely dilated. It would appear that any vigorous manipulation in the region of the hilum of the lung is to be carefully avoided because often this can produce inhibition of the heart.

Whatever is the significance of these phenomena, one cannot deny their existence and their severity. This is one more reason for using beforehand all possible precautions so that one may operate on a wide open chest with the lung collapsed and the patient breathing quietly. The preparatory stages conducive to an uneventful operative procedure and postoperative course will be described subsequently.

*Hemorrhage, Primary or Secondary*—Even with the utmost care and the use of an electric cutting and coagulating instrumentarium, it is impossible to avoid considerable loss of blood in the one-stage operation. The shock due to hemorrhage is added to the shock due to many other causes during operation. The surgeon is obliged to hurry in order to 'get out' of the thoracic cavity before alarming respiratory and circulatory symptoms occur. This question of time is of paramount importance and is well emphasized by Lilienthal<sup>34</sup>. 'I do not believe,' he said, 'I have ever saved one of those patients when in any stage the duration of the operation was more than 45 minutes.' He also stated that cardiac imbalance occurs in proportion to the amount of manipulation required for proper exposure and also in proportion to the time consumed.

It is obvious that by speeding up during the most important stage of the operation, the resection of the diseased lung, one is apt to neglect to perform a careful hemostasis, a meticulous dissection of the pedicle and an accurate closing of the bronchial stump. This makes a secondary hemorrhage more possible and increases the chances of a tension pneumothorax and of severe postoperative infection.

*Increased Intrathoracic Pressure*—Increased intrathoracic pressure due to a tension pneumothorax or a great amount of fluid or both during the first days following operation and the extra work thrown on the heart because of it are other causes of the high mortality in one-stage lobectomy. It is of the greatest importance that one should be able to keep the chest closed in an airtight fashion for from four to seven days after operation in order to induce the remaining lobes of the lung operated on to expand as much as possible. This complication can be avoided to a great extent by careful closing of the bronchus in several layers (Pool and Garlock<sup>34a</sup>). This is possible only if the pedicle has

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<sup>34</sup> Lilienthal H. Thoracic Surgery. Philadelphia: W. B. Saunders Company, 1926, vol. 2, p. 143.

<sup>34a</sup> Pool E. H. and Garlock I. H. Treatment of Persistent Bronchial Fistula. Ann. Surg. 90: 213, 1929.

been well dissected so that one can cut through the stem bronchus and not through the lung, in this way one avoids leaving a more or less considerable part of parenchyma of the lung attached to the lobar bronchus with the possibility that the circular or transfixing ligatures may cut through or release or slide with the resultant opening of tertiary bronchi. When one realizes the tremendous pressure developed during cough as measured by its expulsive force and as is easily seen in a narcotized animal in which one tries to plug a bronchus, one readily understands how a tension pneumothorax, even when due to a leakage through a small bronchial opening can rapidly kill the patient. On the other hand, the amount of intrapleural fluid that always develops after lobectomy and the degree of postoperative, unavoidable infection are proportionate to the amount of infected pulmonary tissue left with the stump. As Brunn well remarked, "the progress of the patient depends on how thoroughly the chest cavity is kept free from air and fluid for the next five to seven days." "Therefore," he said, "I consider the closure of the bronchus a most important step, and it is my endeavor to keep the chest as free from leakage of air as possible during convalescence." But careful closing of the bronchus requires good accessibility of the hilar region and is a time-consuming procedure. So one again comes to the conclusion that in order to make possible a careful dissection of the pedicle and a good closure of it, one needs time and visibility, a combination obtainable only in the graded operation.

#### MULTIPLE STAGE LOBECTOMY

After this study of the pathologic physiology of lobectomy and of the causes of the high mortality incident to it, one may discuss whether lobectomy can become a safer operation than it is now, and how this can be accomplished. I think this can be done by a graded operation in which the successive stages—pneumothorax, phrenicotomy, thoracoplasty and lobectomy—are systematically carried out.

1 *Preliminary Pneumothorax*—Pneumothorax carried on whenever feasible, and for several weeks before operation, is in my mind the most important point in a lobectomy performed in stages. Adhesions in bronchiectasis even in its advanced forms, are generally few. I agree with Lihenthal, who stated that unless exploratory tapplings have been made or an empyema has at some time developed, one should not often find important adhesions binding the bronchiectatic lung to the chest wall. It follows that a good collapse of the lung on the diseased side is generally feasible with artificial pneumothorax. In the first of my cases the roentgenograms clearly showed that a slight pulmonary adhesion had been easily forced by raising the intrapleural pressure to a slightly positive value.

Because of the gradual collapse of the lung of the involved side, bronchial retention and stasis are decreased in proportion to the compressibility of the altered bronchi and parenchyma of the lung. Exceptionally, a kinking of a bronchus may be produced, imprisoning the bronchial exudate, this retention can easily be taken care of, when it occurs, by bronchoscopic aspiration and drainage. As a second advantage, gradual pulmonary collapse produces a gradual decrease in the flow of blood through the collapsed lung, meanwhile allowing a compensatory increase in the flow of blood and ventilation in the other lung as Andrews<sup>35</sup> showed experimentally. In this way, the heart is gradually adapted to the new conditions of respiration and circulation. Churchill<sup>36</sup> showed that the strain on the healthy lung is small and that the circulatory burden thrown on it is not altogether borne by increasing the ventilation but is partly compensated for by an increase in the circulatory area of the lung chiefly through the opening of new capillaries (Wearn, Barr and German<sup>37</sup>). The blood content of the healthy lung is increased as the rate of flow is increased (Drinker, Churchill and Ferry<sup>38</sup>) without marked strain on the heart.

Thirdly, collapse of the lung has as an immediate result a slowing down of the lymphatic drainage of the collapsed lung and of the lymph flow into the blood stream (Naegeli,<sup>39</sup> Dolley and Wiese,<sup>40</sup> Gardner<sup>41</sup>). A decrease in fever and other toxic manifestations follows often accompanied by a marked improvement in the general condition. Moreover this slowing down of lymph flow has as an effect a production of fibrous tissue proportionate to the degree of lymph stasis, such stasis itself being dependent on the degree and duration of pneumothorax. As a result, the visceral and mediastinal pleura become thicker and more resistant, and the mediastinum steadier. Recent adhesions of no consequence for the lobectomy, due to the always present mild infection and irritation of the pleura following pneumothorax, develop and anchor

35 Andrews de W. Observations on Cardiorespiratory Physiology Following Collapse of the Lung by Bronchial Ligation. *Arch Surg* **10** 506 (Jan) 1925

36 Churchill E. D. The 'Strain' on the Collateral Lung in Collapse Therapy. *ibid* **553** (Jan) 1929

37 Wearn J. T. Barr I. S. and German W. T. *Proc Soc Exper Biol & Med* **24** 114 (Nov) 1926

38 Drinker C. K. Churchill E. D. and Ferry R. M. *Am J Physiol* **77** 59 (Aug) 1926

39 Naegeli. The Changes of the Serological Reaction of the Blood After Extrapleural Thoracoplasty (quoted in Dolley & Wiese footnote 40). *Beitr z klin Chir* **90** 351 1914

40 Dolley, F. S. and Wiese R. E. Effects of a Large Closed Bilateral Pneumothorax on Thoracic Lymph Flow. *Arch Surg* **18** 542 (Jan) 1929

41 Gardner L. V. The Pathology of Artificial Pneumothorax in Pulmonary Tuberculosis. *Am Rev Tuberc* **10** 501 1924

the mediastinum and thus increase its stability. Furthermore, prolonged pneumothorax decreases the secretory and absorbing capacities of the pleura.

2 *Phrenicectomy*—Phrenicectomy, performed as a second stage, is an excellent addition to pneumothorax and a valuable aid in obtaining further collapse and immobilization of the lung, particularly because of the predilection of bronchiectasis for the lower lobes. Alexander<sup>42</sup> considered that the paralysis of the diaphragm acts more by immobilizing than by causing further collapse of the lung. This is shown by the marked improvement even in cases of bronchiectasis, as well as in those of tuberculosis, in which the base of the lung and the diaphragm are immobilized by strong adhesions and in which no appreciable elevation follows the operation. It is obvious that in these cases paralysis of the diaphragm acts only by further immobilization of the lung. Preliminary pneumothorax carried on for a sufficient time and followed by phrenicectomy requires that the patient accommodate himself to breathing with only one lung; it steadies the mediastinum, produces thickening of the pleura and decreases the absorption from the serosa.

3 *Thoracoplasty*—These results are further enhanced by extra-pleural graded thoracoplasty limited to the affected area and performed in as many stages as are necessary. Thoracoplasty as a preliminary stage is extremely valuable. Not only does it further increase the collapse of the lung, especially when pleuropulmonary adhesions are present and pneumothorax is not successful, but it decreases the capacity and depth of the thoracic cavity. After thoracoplasty has been performed, the fourth stage of the operation, namely, exploration of the lung and its resection, is greatly simplified, no time is spent in the resection of ribs and opening of the thoracic wall, no hemorrhage is produced, the wall has lost its rigidity and can easily be retracted and the hilar portion of the lung is accessible because the collapse of the wall has brought this region nearer to the surface. Last but not least, the remaining lobe, on expanding, can more readily fill up the reduced thoracic cavity and thus shorten the time for anatomic and physiologic recovery.

It is really impressive how lobectomy becomes a relatively easy operation after these preliminary stages, pneumothorax, phrenicectomy and thoracoplasty, especially because of the absence of disturbances of respiration and circulation. When, after these stages have been performed, the chest is opened, the patient breathes as if the chest were closed. It is astonishing, as Eloesser remarked, to see the patient breathing quietly with the thoracic wall wide open and the homolateral lung completely collapsed. A collapsed lung and quiet respiration give

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<sup>42</sup> Alexander J. in discussion of Dolley and Wiese (footnote 40, p. 552)

plenty of room to operate and perfect visibility—a perfect combination for a quiet and accurate operation. Separation of the affected lobe from adhesions, isolation of its pedicle, clamping of vessels and careful closure of the stump after resection can all be performed with surprising ease, and ease in lobectomy makes for accuracy and speed.

Thus the principal dangers in lobectomy are eliminated or greatly palliated—namely, shock, cardiac failure, reflex inhibitory phenomena and hemorrhage. A careful dissection of the pedicle allows cutting of the bronchus and no cutting through the lung tissue, thus almost no infected pulmonary parenchyma is left in the stump. This lessens the degree of postoperative infection in the thoracic cavity, which should be closed in an air-tight manner, permits one to keep the thoracic cavity closed for several days and thus allows the remaining lobes to expand. Lastly, reduction in the size of the thoracic cavity due to the thoracoplasty makes its filling with expanded lobes more feasible, pleural sinuses tend to disappear and bronchial fistula tends to heal promptly.

By the use of the technic described, opening of the chest becomes almost no more troublesome than laparotomy. With respiratory and circulatory functions undisturbed, one is able to operate on intrathoracic organs as on intra-abdominal organs, the resection itself of the diseased lung being reduced to almost a minor operative procedure. The presence of extremely strong adhesions intimately uniting the lung to adjacent lobes, parietal pleura and diaphragm may render separation of the bronchiectatic lung impossible. Such adhesions are rare and are generally observed in bronchiectasis following empyema. These adhesions are suspected when repeated attempts at pneumothorax have been unsuccessful. In these cases, lobectomy may be impossible, and cauterized pneumectomy then is the method of choice. Even in the cases in which a separation of the affected lobe has been possible but has required prolonged manipulation, one should not consider it wise to perform lobectomy at this stage. In these cases, two procedures may be employed. The lobe may be covered completely with a large piece of rubber tissue after having been separated from the adjacent structures—lung, diaphragm and parietal pleura and the thoracic wall accurately and completely closed and air-tight tube drainage of the pleural cavity instituted. From four to ten days later, the cavity is reopened and the lobe resected, following the technic advised by Lilienthal,<sup>34</sup> or, after separation of the bronchiectatic lobe from the adjacent lobe, the branch of the pulmonary artery is found and ligated. The last procedure was advised by Bruns and Sauerbruch<sup>43</sup> who from experimental results

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43 Bruns, O., and Sauerbruch, F. Die künstliche Erzeugung von Lungenschwund durch Unterbindung von Ästen der Pulmonarterie. *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **23** 343, 1911.

concluded that it could serve as a curative procedure for bronchiectasis. It is known that ligation of a lobal pulmonary artery produces atelectatic shrinkage of this lobe with subsequent development of connective tissues and fibrotic sclerosis of the pulmonary parenchyma. Unfortunately, this sclerosis is not sufficient to produce complete collapse and closure of the dilated bronchi because of the induration of their walls. Sauerbruch<sup>14</sup> used this method in fourteen cases of advanced bronchiectasis, without any definite results. In six of these cases, thoracoplasty and lobectomy were later performed. Ligation of the pulmonary artery is technically easy in the inferior lobes and is an excellent preliminary measure in the cautery pneumectomy of Graham,<sup>15</sup> when feasible, because it eliminates the dangers of hemorrhage and an or septic embolism in this otherwise excellent method.

It is even possible that ligation of the pulmonary artery in cases of uncomplicated unilateral bronchiectasis might prove a curative method when combined with thoracoplasty.

Whittemore<sup>20</sup> described and successfully performed exteriorization of the affected lobe after resection of several ribs. He liberated and delivered as much of the lobe as possible out of the chest and fixed it there by suturing it to the muscles of the thoracic wall. After a variable time, the exteriorized lobe became necrotic and sloughed away. Five of six patients on whom he performed the operation were clinically cured; the sixth died. There is no doubt that this procedure has some marked advantages over lobectomy and deserves a serious trial. It is not within the scope of this paper to enter into details, it aims only to show the marked advantages of a graded lobectomy in which the successive stages are systematically performed in the order described.

There are authors who still advocate the use of the one-stage operation. Lately, Brunn,<sup>17</sup> in a paper read before the American Association for Thoracic Surgery, reported six cases with five cures and only one death. Although I greatly appreciate these results and the skill of the operator and I profess the greatest admiration for the pioneer work of Sauerbruch and Lahenthal, I confess that I believe that graded lobectomy is a much safer operative procedure.

The two cases reported here are offered in support of these views.

#### REPORT OF CASES

Two cases only are given and these are chosen because the operations in both were performed over two years ago, hence one may judge of the late results. The other cases will be reported in a forthcoming paper. Thus far there has been no mortality during the last stage.

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44 Sauerbruch (footnote 21 vol 2 p 572)

The first was a case of advanced bronchiectasis in a girl of 18, with multiple abscesses, foul expectoration and extreme emaciation. Bronchial dilatation was present in both lungs but showed a marked predominance in the left lower lobe. A multiple stage lobectomy as described was performed and was followed by a complete and definite cure. The second was a case of advanced bronchiectasis, developed after pneumonia with empyema for which repeated operations had been performed. Bronchiectatic abscesses were spread over the whole right lung and were accompanied by foul sputum, fever and extreme emaciation. The same preliminary procedures except pneumothorax, were carried out but instead of lobectomy, cauterization and pneumectomy was performed. Complete clinical cure followed, with a small bronchial fistula purposely maintained and actually almost dry. This patient at the time of writing was perfectly well although in the seventh month of pregnancy.

**CASE 1—History**—M. K., a white girl, aged 16, entered the medical ward of Bellevue Hospital, 2nd Division (Cornell) on March 28, 1928. Her chief complaint was persistent cough, abundant purulent, foul expectoration, loss of weight and general exhaustion. In June, 1928, she had a severe cold, diagnosed as pneumonia. After three weeks, she improved but did not get rid of the cough. In September, 1927, she began to expectorate large amounts of greenish purulent, foul sputum. Although she had postural drainage three times a day for the four months preceding admission, the amount of sputum gradually increased from 8 ounces (236 cc.) to from 15 to 20 ounces (444 to 592 cc.) daily. She lost 32 pounds (14.5 Kg.) in one year.

She had been told that she had had pneumonia in infancy. She had always been subject to colds and cough.

**Physical Examination**—The patient was emaciated and looked exhausted. The skin was dry, the membranes were pale. The teeth were bad. The sinuses examined by a member of the staff of the nose and throat department, were found healthy. The left side of the chest was diminished in size and excursion, and appeared flat in comparison with the right. The heart was normal, though slightly displaced to the left. The right lung was normal. On the left side, dullness was present posteriorly from the fifth intercostal space down to the base of the lung where breath sounds tended to be bronchial. Vocal and whispered fremitus was increased all over the left lung, especially at the base posteriorly, and in the axillary line. Many râles were heard at the left base, less in the right lung. The abdomen appeared normal. The fingers and toes were markedly clubbed and slightly cyanotic. The temperature varied from normal to 102° F., the pulse rate was from 80 to 120. The Wassermann reaction was negative.

The sputum amounted to from 12 to 18 ounces (355 to 532 cc.) daily. It was greenish, separated in three layers and of extremely foul odor. It showed streptococci, staphylococci, diplococci, spirochetes and large bacilli but no tubercle bacilli, and occasional red cells.

Bronchoscopic examination showed (April 12, 1928) pus coming from the left lower lobe and to a lesser degree from the right lower lobe.

A roentgenogram showed a definite process in the left lower lobe (with mottled shadow), increased pulmonary markings in both hilar regions, especially on the left (fig. 1).





Fig 1 (case 1) —Bronchiectasis, especially marked on the left lower lobe (April 10, 1928)



Fig 2 (case 1) —Bronchography (lipiodol) showing bronchiectasis of left lower lobe

*Pneumothorax*—Pneumothorax was done (April 14) and the lung maintained collapsed for one month by adequate refillings. There were few pleuropulmonary adhesions (fig 2), which were gradually forced (fig 3) by increasing the intrapleural pressure (4641) so that the collapse became complete (fig 4) within four weeks.

During this time (from April 14 to May 15, 1928), the general condition improved: expectoration diminished from 15 to from 2 to 4 ounces (from 444 to 59 to 118 cc) daily, the sputum decreased and the temperature returned to normal; the patient had gained 12 pounds (5.4 Kg). She was discharged and was instructed to come regularly every week for refilling, thus she neglected to do. When she came back June 12, 1928, she was in the same condition as before pneumothorax, if not worse. The temperature oscillated between 100 and 102 F, the pulse rate around 120. There was a continuous exhausting cough with foul expectoration of



Fig 3 (case 1)—Refilling kept on, incomplete collapse (April 23, 1929)

from 10 to 18 ounces (from 295 to 532 cc) daily. Roentgenograms before (fig 5) and after (fig 6) injection of iodized oil taken the same day, showed that cylindric and saccular dilatations of the bronchi in the left lower lobe had not been influenced by the collapse of the lung. The patient was placed in the service of Dr. Alexander Miller of Bellevue Hospital for observation. A lobectomy was decided on, and the patient was transferred to the surgical ward.

Pneumothorax was started again with refillings every three days. No adhesions developed, and the lung had again collapsed completely (fig 7). The vital capacity on June 22 was 1,900 cc. On June 25 the red cells numbered 3,100,000, the hemoglobin content was 60 per cent. The white cells numbered 12,500. A transfusion of 500 cc of whole blood was given.

*First Operation*—On June 26, 1928, a partial thoracoplasty was performed, with resection of the posterior part of the six inferior ribs, the patient being under high spinal anesthesia.

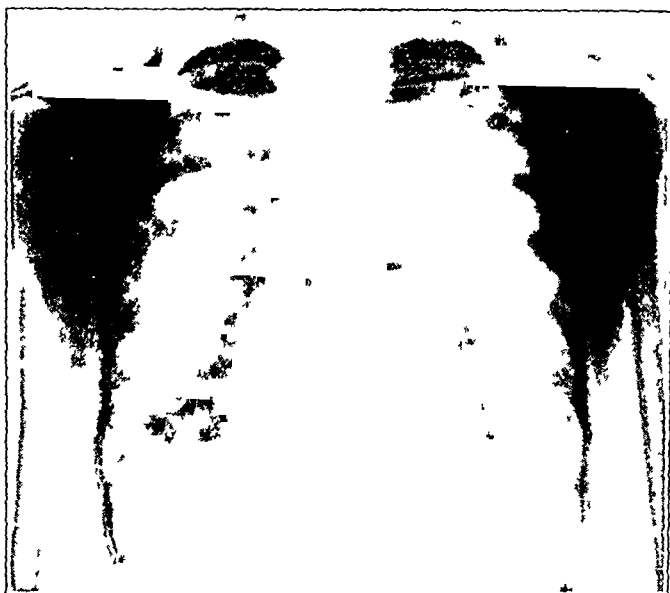


Fig 4 (case 1)—Collapse complete The pleuropulmonary adhesions have gradually yielded (May 4, 1928)



Fig 5 (case 1)—Patient neglected to come weekly for refilling for one month and a half The upper lobe is still collapsed, but the lower lobe is again visible (June 12, 1928)

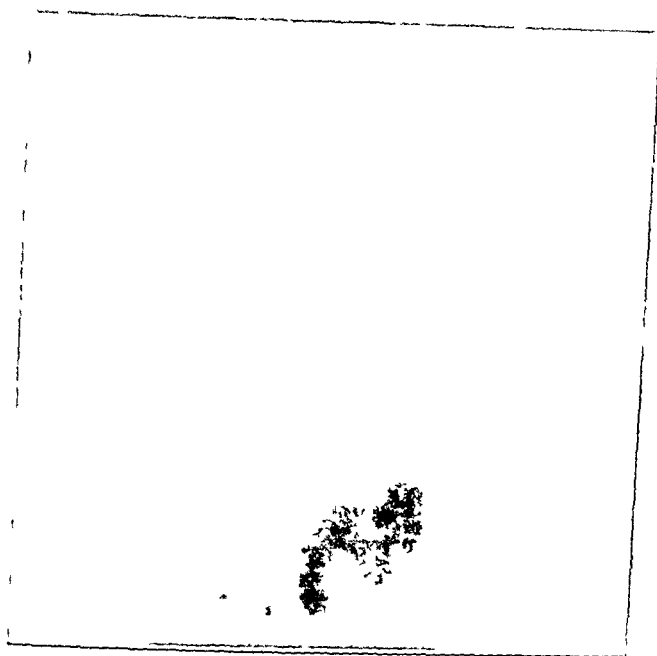


Fig 6 (case 1)—An injection of iodized oil shows cylindric and saccular bronchial dilatation of the left lower lobe (June 12 1928) (unsuccessful radiogram)



Fig 7 (case 1)—After artificial pneumothorax, the left lung is completely collapsed, showing absence of adhesions, although the lung was permitted to expand after the previous pneumothorax. The roentgenogram was taken on June 22, 1928.

**Anesthesia** Three grams of phenobarbital was given half an hour before operation. Morphine was not used. Caffeine and sodium benzoate, 75 grains, were given fifteen minutes before spinal anesthesia, and one ampule of ephedrine. Spinal anesthesia was obtained with 70 mg of procaine hydrochloride. The patient sat with the head in forced flexion. The space between the fourth and fifth thoracic vertebrae was located and local anesthesia was obtained with 1 per cent procaine hydrochloride injected by means of a fine long needle inserted first horizontally then obliquely upward. The spinal fluid readily started flowing. The 70 mg of procaine hydrochloride (Corbiere) in crystals was dissolved in 2 cc of cerebrospinal fluid and slowly injected. No cerebrospinal fluid was allowed to flow out. The patient was left in sitting position for a few seconds and then placed flat, with the head lower than the body. Analgesia was complete from the chin to the umbilicus in about two minutes. Below the umbilicus no anesthesia of any kind (to pain, heat or cold) was present. In the arms there was complete analgesia without any motor impairment. No dyspnea or other subjective or objective respiratory disturbances were noticed, nor were there any disturbances in rhythm and rate. Blood pressure dropped within ten minutes after anesthesia from 110 systolic and 60 diastolic so as not to be recordable. The pulse was rapid and weak, but both were improved within twenty minutes after the injection. No additional ephedrine was given.

**Operative Procedure** A paravertebral incision was made on the left side, 8 cm from the line of the spinal apophyses, beginning at the fourth intercostal space, down to the eleventh and curved forward following this space, to the anterior axillary line. Incision of skin and muscle was done. A musculo-cutaneous flap was separated by blunt dissection, and the seventh, eighth, ninth, tenth, eleventh and twelfth ribs were resected from the transverse apophyses to the middle axillary line. The pleura opened accidentally above the twelfth space. Because of the already existing collapse of the lung, no disturbance whatever occurred after this pleural opening, which was immediately sutured, the intercostal blood vessels were ligated and the nerves were injected with alcohol 95 per cent, according to the technic of Hedblom. A small cigaret drain without a gage was placed under the muscles. Catgut sutures were done on the muscles, silkworm tension sutures inserted and Michell's clips placed on the skin. A dry dressing was applied. The patient was returned to bed in fair condition. The duration of the operation was forty-five minutes. At the end, slight gas-oxygen anesthesia was given, the patient feeling no pain but complaining of a "pulling up" of the ribs during their resection. Suturing required additional local anesthetic.

**Postoperative Course** The postoperative course was rather stormy. The temperature went up to 105 F, the pulse to 140. The patient expectorated 18 ounces (532 cc) of foul sputum in the evening and was greatly relieved. The temperature was normal on the third day. On the fifth day, the patient got out of bed. The cigaret tube was taken out the third day. The wound healed by primary union, the cough decreased, the sputum did not exceed from 2 to 4 ounces (59 to 118 cc). Figure 8 shows the roentgenogram taken on the tenth postoperative day, just before the second operation.

**Second Operation**—The second operation was performed on July 7, 1928. This was a second stage thoracoplasty, with resection of anterolateral portions of the same ribs with cartilaginous border, the patient being under high spinal anesthesia. Anesthesia was produced by the same procedure as had been used previously. The same results were noted and the same drop of blood pressure with rapid recovery (in sixteen minutes) followed.

**Operative Procedure.** A long incision was made from the fifth intercostal space 2 cm. to the left of the sternal border, long parallel to the sternal border and curved to the median axillary line following the costal border. An incision of 10 cm. was made. Direction and restoration of the whole length of the costal border and of the remains of the anastomosis which had severed ribs had been effected in the previous stage was done from their union to the median axillary line. By the same procedure the rib was resected from the sternal border to the posterior axillary line. During the liberation of the costal border the pleura was opened by an incision 3 cm. in length without any disturbance of the respiration. It was immediately closed by continuous suture with plain catgut. Suture of muscles by layers followed after circular hemostasis. A rubber dam was introduced under the muscular layer. Retention sutures (silk 3/0) were used, the skin was sutured with plain silk. A dry dressing was applied. The patient was sent to the ward in excellent condition. The duration of the operation was fifty minutes. During the last fifteen minutes a slight amount of gas oxygen in oxygen was given.

**Postoperative Course.** The postoperative course was smoother than that after the first stage. On the seventh postoperative day there was an elevation of the temperature because of infection of the wound in the lower angle. After drainage the temperature subsided. On July 16 the red blood cells numbered 3,200,000; the hemoglobin content was 50 per cent. A transfusion of 500 cc. of whole blood was given.

The patient was out of bed on July 21 and the wound was completely healed on August 2. The patient gained 4 pounds (1.8 Kg.); the cough and expectoration were markedly decreased but still persisting especially during the night. The blood, August 6, showed red cells 4,100,000; hemoglobin 65 per cent.

**Third Operation.**—On Aug. 8, 1928 (one month after the second operation), a lobectomy of the left lower lobe was done.

**Pathologic Changes in Left Lower Lobe.** The excised left lower lobe presented the blue-black color of an atelectatic lung but it was elastic not friable crepitant, and did not sink in water, on pressure mucopurulent froth came from the sectioned bronchus. The lobe was strongly adherent to the diaphragm and to the posterior wall. There were adhesions between this lobe and the upper lobe which were of recent formation.

**Anesthesia.** High spinal anesthesia was produced with 80 mg. of procaine hydrochloride in 2 cc. of spinal fluid injected into the fifth dorsal space. Immediately after the injection and for about two minutes thereafter there was slight respiratory distress. The patient complained she could not catch her breath. There was no acceleration or slowing of the respiration. Immediately after injection, a complete anesthesia developed from the sixth cervical vertebra down to the twelfth.

The blood pressure taken every ten minutes during anesthesia, showed a drop of 50 points in the first ten minutes after anesthesia, from 110 systolic and 65 diastolic to 60 systolic and 0 diastolic, but fifteen minutes later, it was above normal, 120 systolic and 80 diastolic and was maintained there until the end of the operation.

**Operative Procedure.** A long incision of the skin was made following the seventh intercostal space. Division of muscles and hemostasis followed. The ribs were represented by cartilaginous tissue, which shows how quickly the ribs are reformed. The cartilaginous tissue was cut with the knife and the pleura opened wide from almost the sternal border to the postaxillary line. Lihenthal's retractor

was inserted, and the incision stretched. At no time was there any respiratory disturbance from the opening of the pleura. The patient continued to breathe quietly as before. The lower lobe presented the characteristics described. The lung was gently secured with Tuffer's special clamps and pulled out. The heart, the upper lobe and posteriorly the aorta and esophagus, were seen, as well as the left phrenic nerve. The adhesions to the upper lobe were separated with the finger, the pericardiopulmonary ligament was sectioned and the base of the lung slowly and laboriously liberated from the diaphragm. Two curved nephrectomy clamps were placed on each side of the bronchus, which had been dissected almost free from the pulmonary parenchyma. Traction on the bronchus was carefully avoided. On the proximal side of the clamped bronchus, silk ligatures were placed, transfixing the bronchus. Vessels were ligated separately. The clamps were removed after the section of the bronchus, and the stump of the bronchus was carefully closed with interrupted catgut sutures through the perichondrial tissues. In the center of a rubber dam 12 inches square (77.4 cm.), a small hole was made and the long threads of the ligatures passed through it, and the stump of the lobe also was forced through the opening (Lilienthal). Iodoform gauze packings were placed in contact with the stump inside of the rubber dam, the threads of the ligatures fixed on a big safety pin and left long enough to reach the thoracic wall, when slight tension was exerted on it. In the lower part of the thoracic wall and midaxillary line a small hole was made. A rubber tube, 30 French, was introduced (air-tight) and fixed to the skin by silk string suture. Rubber dams and packings were left in the chest, the pleura was sutured with interrupted catgut sutures above them, and only the safety pin was left outside of the pleura. The muscles were sutured with interrupted catgut covering the safety pin, the position of which was marked by a small incision in the skin. Suture was on the subcutaneous tissues. No sutures were placed on the skin. A petrolatum gauze dressing was applied to the wound and covered with dry gauze. The lower drain was connected with a tube, the end of which was introduced into a bottle half filled with water in order to insure air-tight drainage. The excised lobe was sent to the laboratory. The patient was sent to the ward in fair condition. The duration of the operation was one hour and twenty minutes.

**Postoperative Course.** Seven and a half grains of caffeine, one ampule of digifolin and morphine  $\frac{1}{4}$  grain, were given every six hours. On the day after the operation a transfusion of 500 cc of whole blood was given.

The patient withstood the operation in a really remarkable way. There was little postoperative shock, and on the second postoperative day, the patient was sitting up in bed.

The first dressing was done on July 11 (third postoperative day), the sutures were cut and the thoracic cavity opened. Little, if any, infection was observed and no foul odor, 4 ounces (118.29 cc) of dark serous fluid came out. The safety pin holding the silk sutures was located. The rubber dam was found. The iodoform gauze packing was extracted and new iodoform gauze lightly packed in, the thoracic cavity was closed with two silkworm sutures. A wet dressing sealing the opening as completely as possible was applied, on this a rubber dam was placed. The lower tube was perfectly airtight and draining fairly well.

Dressings were done every second day by changing the iodoform packing inside the rubber dam, which was left in place for twelve days. No washing or irrigation of any kind was used. The lower drain was taken out on the sixth day, on the twelfth day, the rubber dam was taken out. The silk ligatures of the pedicle were still holding. The wound led into a cavity, the size of an orange, clean,

abundantly cultivated to clear and in any foul odor and almost no suppuration. Iodoform gauze was loosely placed into the cavity. The approximate capacity was 150 cc.

On the nineteenth day after operation the stump of the pedicle sloughed away. A slight wheeze (bronchial fistula) could be heard only when the patient coughed. By the twenty-fifth postoperative day the cavity had greatly diminished. Still wheezing occurred only on coughing. There was no bubbling when the cavity was filled with saline solution on ordinary respiration. The patient was out of bed on the twenty-seventh day. The capacity of the cavity was then 20 cc. The same day a roentgenogram (fig. 8) was taken. The general condition of the patient was excellent. At this time the patient was gaining a pound (0.5 Kg) a day.



Fig. 8 (case 1)—Seven days after graded lobectomy of the left inferior lobe. Seven inferior ribs were resected previously. The postoperative cavity is clearly seen.

On the thirtieth day, the capacity of the cavity was 10 cc. There was no bronchial fistula. The patient was discharged on the thirty-eighth day and directed to come to the ward for dressing. On the fiftieth day the wound was completely closed. There was no bronchial fistula.

A dry cough persisted for two days following operation. Expectoration ceased completely after operation. From the third day on there was no cough or expectoration, nor was there any at the time of writing.

The patient had gained 35 pounds (15.9 Kg) by Dec. 15, 1928, four months after the operation. At the time of writing she was perfectly well, did not cough or expectorate, and was working as a switchboard operator.

The last roentgenogram (fig. 9) was taken in March, 1929, showed that the upper lobe was expanded and was about two thirds the size of the right lung. At that date, the patient weighed 122 pounds (55.3 Kg), a gain of 52 pounds (23.6 Kg) since operation, the vital capacity was 3,400 cc.



An x-ray picture on Oct 15, 1926 showed in the lung, an area of consolidation with several areas of excavation at the base occupying the third, fourth and fifth interspaces, the diaphragmatic outline and the costophrenic sinus of the seventh rib partially obliterated, apparent resection of the seventh rib posteriorly.

Diagnosis Lung abscess (The roentgenogram was lost)

On Oct 21, 1926 (six months after the first operation) the patient reentered the hospital. So long as the tube was kept in the sinus after the last operation, the patient was comfortable and had little cough. In September, the tube was removed and when the wound healed, she began to cough and expectorate foul sputum as before.

*Second Operation*—The second operation was performed on Oct 29, 1926, by Dr Shepard, the house surgeon.

*Pathologic Changes* The site of the rib resection at the seventh rib had been filled in with cartilage, partially calcified in places. The hiatus in the ninth rib was filled with scar tissue. There was an area of consolidation of the lung just medial and slightly posterior to the site of excision of the seventh rib.

*Operative Procedure* With the patient under local anesthesia produced with 1 per cent procaine hydrochloride, an incision was made through the scar tissue in the region of the ninth rib, and the pleura at this point. The pleura was free just above the opening, however, were adhesions between the thoracic wall and the consolidated area of the lung which has been described. A parallel incision was then made over the region of the seventh rib, and a portion of cartilage excised. Through the opening thus made, a trench was opened into the consolidated lung by blunt dissection. This was extended to the limit to which the gloved finger could be introduced and was packed with iodoform gauze. A small rubber drain dam was inserted in the anterior angle of the lower wound, which was then closed with chromic and interrupted catgut, the latter half of the operation was performed with the patient under gas-oxygen anesthesia.

*Postoperative Course* The padding inserted at operation was all removed on November 7 (nine days after operation) and a large rubber drain was inserted. A definite bronchial fistula was noted at that time. On November 9, a probe was introduced into the trench made at operation and an x-ray picture taken, which was reported on as follows: "The probe enters the abscess cavity which extends almost to the hilum. The lateral plate shows beginning sclerosis of the walls of the cavity." On November 14, the large tube was removed and a small rubber tube was inserted. The patient was referred to the nose and throat department, where it was noted by those who examined the patient that both antrums were dark, treatment was instituted. The patient was discharged markedly improved and was advised to keep the tube for several months.

On Jan 6, 1927, the patient was admitted for the third time. She complained of weakness and swelling of the ankles about four weeks previous to admission. She had had moderate cough and foul expectoration since her discharge, although the tube had been left in place. The examination of the blood red cells 3,800,000, hemoglobin content 58 per cent. A transfusion of 500 cc was performed, following which the hemoglobin rose to 65 per cent and the number of red cells to 4,200,000. An x-ray picture following injection of iodized oil into the sinus showed "Multiple pulmonary abscess cavities communicating with the bronchus." The patient was discharged, January 10, on her demand, slightly improved.

On June 21, 1927, the patient came to the hospital because for seven weeks she had been coughing frequently and expectorating foul sputum (from 2 to 5 ounces [59 to 148 cc] daily), although the drain tube was in place. She at first gained 15 pounds (6.8 Kg), but lost it within the seven weeks.

At the first operation the patient had for the first time. She looked emaciated and had already lost a great deal of weight and expectorated foul sputum. The temperature was 104.1° F. on July 1, 1927. Respiratory rate 20 to 25, weight 75 lbs. On July 5, 1927, a hypodermoclysis employing injection of dextrose 25 per cent was given. The patient improved and the temperature dropped to 101.5° F. The upper limit of the cavity reached at the first operation was 15.24 cm. A graded thoracoplasty was decided on. The patient was discharged with a stage.

**First Stage.** On July 5, 1927, with the patient under gas-oxygen-ether anesthesia a paravertebral incision was made extending from the seventh to the second rib were resected. The first rib was left because of the alarming condition of the patient at the end of the operation. From 3 to 6 inches (7.6 to 15.24 cm) of each rib was resected. The postoperative course was smooth. The wound healed within ten days.

**Second Stage.** On July 18, 1927, with the patient under gas-oxygen-ether anesthesia a paravertebral incision was made extending from the lower end of the incision of the previous operation downward to the eleventh rib and then outward following this rib to the anterior axillary line. The eighth, ninth, tenth and eleventh rib were resected from their angle to the costal cartilages.

**Second Postoperative Course.** The patient had a severe reaction, the temperature rising to 105.5° F. with a great deal of respiratory distress. Her condition gradually improved. A hypodermoclysis employing dextrose and saline solution was done. An intravenous injection of dextrose 25 per cent was given and on the fifth day a transfusion of 500 cc of blood was employed. The patient responded extremely well to these measures. The wound of the thoracoplasty was infected and healed slowly by granulation. The tube was maintained in place.

The patient was discharged twenty-seven days after the second stage, markedly improved, the cough was diminished and expectoration was from 2 to 3 ounces (59 to 88 cc) in twenty-four hours. The right side of the chest was markedly collapsed. The patient was told to come for dressings. It was explained to her that several operations would be necessary for complete cure.

**Third Stage.** On Oct 30, 1927, a parasternal incision and resection of the remaining anterior segments of the second, third, fourth and fifth ribs was performed and also phrenicectomy of the right phrenic nerve.

**Third Postoperative Course.** A perfect collapse of the chest followed this operation. The postoperative course was smooth, the temperature oscillated between 100 and 101.5° F. for four days, then gradually returned to normal. A great amount of foul sputum was evacuated during the first five days, then the amount decreased rapidly and thirteen days later, when the patient was discharged, she had only a slight cough and expectoration of from 1 to 2 ounces (30 to 59 cc) of slightly foul sputum. The wounds of the thoracoplasty and of the phrenicectomy were healed.

An x-ray picture taken on Nov 11, 1927, showed "Right lung completely collapsed, dense fibrosis of the base." One month later, on Dec 13, 1927, an x-ray picture was taken after injection of iodized oil through the trachea. The report was "Base shows complete fibrosis, upper lobe is collapsed with bronchiectatic cavities."

By this time, the patient had put on 9 pounds (4.1 Kg) since the last operation. But the cough persisted with expectoration of from 1 to 2 ounces (30 to 59 cc) of foul sputum in twenty-four hours. Besides, although the lower lobe did not show any cavities and had undergone almost complete fibrosis, bronchiectatic cavities appeared in the upper lobes.

**Fourth Stage** The patient was admitted on Dec 18, 1927 and given a transfusion of 700 cc of whole blood. The fourth stage of the operation was performed on Dec 20, 1927.

**Pathologic Changes** The thoracic wall was collapsed and all the ribs resected, except the first, in previous operations. The lung was collapsed, dark and adherent to the parietal pleura, the distinction of the different lobes was difficult. A number of cavities of sizes varying from a walnut to a hazelnut and smaller, were found in the pulmonary parenchyma of the three lobes, containing foul smelling fluid and gangrenous tissue. It was felt that there were still other cavities present.

**Operative Procedure** With the patient under gas-oxygen-ether anesthesia, a horse-shoe incision was made, going from the anterior axillary line and the second space downward to the level of the tenth rib and then upward and backward to the third space, on the spinal border of the scapula. The chest flap, composed of skin and muscles, was reflected upward, and the pleura, completely adherent to the underlying collapsed lung, exposed. A soldering iron, heated to cherry red, was plunged into the parenchyma of the lung and the cavities mentioned, opened. Four cauterizations were made, the iron penetrating each time to a depth of from  $1\frac{1}{4}$  to 2 inches (3.1 to 5 cm). The moderate hemorrhage was easily checked by packing. A Mikulicz rubber pad was inserted and solidly packed with iodoform gauze. The flap was deflected and temporarily sutured with two sutures of silkworm gut only.

**Fourth Postoperative Course** The postoperative course was remarkably smooth. The temperature did not rise above 101 F, cough and expectoration greatly decreased.

The cauterization of the lung was repeated on January 4 and 11. In each stage, new abscesses were opened. The moderate hemorrhage was easily checked by compression. The wound was left open and packed with a large piece of rubber dam containing iodoform gauze.

After the third cauterization, the patient's condition showed a remarkable improvement. The cough and expectoration ceased completely, the wound was clean, showing a great number of bronchial orifices on its surface, gangrenous tissue was eliminated and healthy granulations were filling up the wound. The foul odor had disappeared. The dressing with the rubber pad tightly packed with iodoform gauze was kept on. The patient was discharged on Jan 28, 1928, and instructed to come every day for dressings.

By March 1, 1928, the wound had gradually decreased in size, showing bronchial orifices in its depth, from which air was freely going in and out. The cough and expectoration had disappeared completely. There was no foul odor or taste in the mouth. There was little discharge from the wound. The patient gained 20 pounds (9 Kg) in three months and felt fine, perfectly well and happy. A tube was inserted in the orifice to avoid possible closing. A roentgenogram (fig 11) showed the lower lobes fibrotic and opaque. The upper lobe was slightly aerated. The iodized oil was still visible in the bronchi.

On June 19, the improvement was maintained, the weight was increased. The wound was small, about the size of a pencil. With the thoracoscope introduced in the orifice of the fistula, four bronchial openings, well epidermized, were seen. A roentgenogram (fig 12) showed an advanced aeration of the upper lobe with absence of any indication of abscess.

On Aug 20, 1929, the patient felt perfectly well, did not cough or expectorate, and performed her duties of mother and housekeeper. She was in the seventh month of pregnancy. A tube the size of a Dakin tube was still maintained in

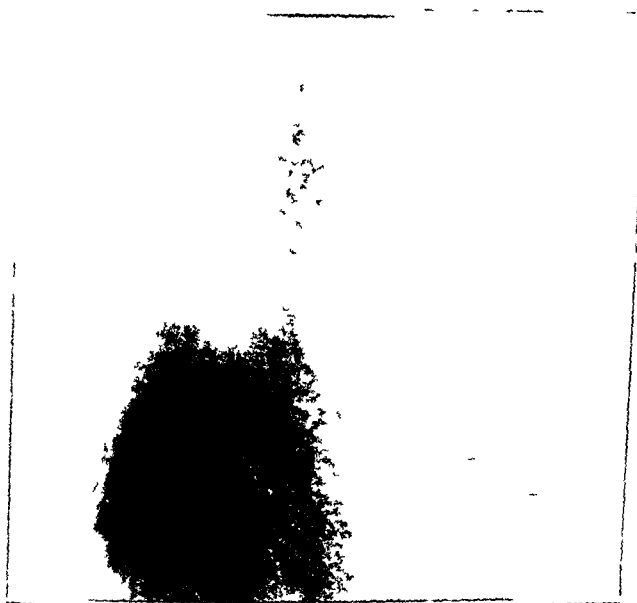


Fig 11 (case 2)—Graded thoracoplasty, phrenicotomy and cautery pneumocotomv, forty-eight days after the last stage (March 1, 1928)



Fig 12 (case 2)—Seventeen months after operation. The remainder of the right lung has expanded in the upper part of the right side of the chest (June, 1929)

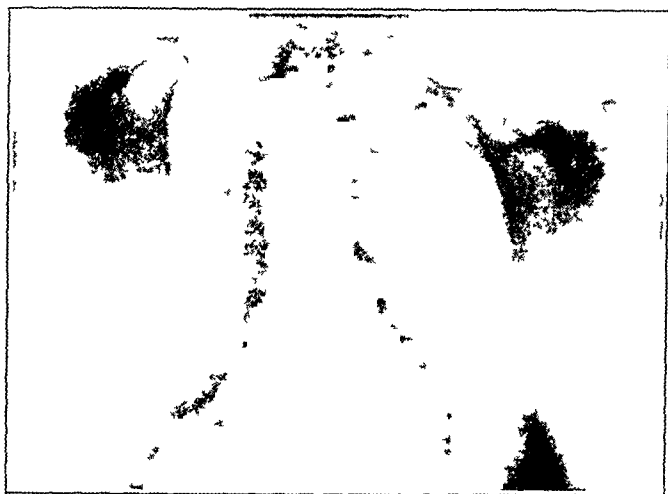


Fig 13 (case 2) —Twenty months after operation Expansion of the remaining parenchyma of the lung is still more accentuated on the side operated on (September, 1929)

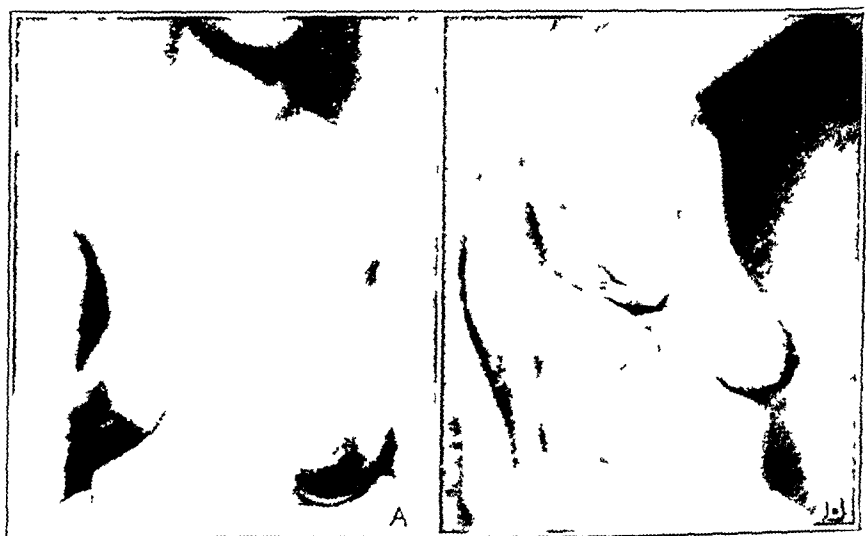


Fig 14 (case 2) —Photographs taken two years after pneumectomy

place, although there was no more discharge. The patient had gained 39 pounds (17.7 Kg) since being discharged from the hospital. A roentgenogram (fig 13) showed a remarkable progress in the re-aeration of the remaining parenchyma of the right lobe which filled up what was left of the thoracic cavity on the side that had been operated on. On Jan 4, 1930 the patient was in perfect condition. She had a normal delivery of a healthy baby weighing 6 pounds (2.7 Kg), which she was nursing. (The first roentgenograms taken of this patient's lungs were lost. Only the three last are shown here.)

#### COMMENT

The two cases presented have several points of interest.

The first was a typical case of bronchiectasis of undetermined origin possibly resulting from pneumonia in childhood, with frequent coughs and colds since. After every cold the chronic condition presented a temporary exacerbation which was followed by permanent aggravation of the existing condition. Finally a more severe pulmonary attack produced the classic symptoms of advanced bronchiectasis. A roentgenogram taken following the injection of iodized oil, several years ago, would certainly have shown bronchial dilatation already present, and a bronchoscopic examination at that time probably would have revealed incomplete drainage and possibly retention in the bronchi of the lower left lobe. Another point of interest is the absence of pleuropulmonary adhesions, although the bronchial dilatations were of considerable size and the fact that even after the refillings were interrupted for over a month, no adhesions developed. The collapse of the lung, which had been complete for about two months was followed by a marked improvement of only temporary duration.

Another fact of great importance is that this patient presented rather advanced lesions at the right base besides the main lesions on the left to such an extent that Dr. A. Miller was doubtful as to the indications for, and the outcome of a lobectomy. However the lesions on the right side cleared up shortly after the excision of the principal focus (left lower lobe) and gradually disappeared completely.

The method of obtaining the high spinal anesthesia in this case is not above criticism. I used it because of the great satisfaction it gave me in an extended experience during the Great War. I was then the first to use procaine hydrochloride instead of benzocaine dimethylaminoethylpropanol hydrochloride (stovaine) which Jonesco, the pioneer in the use of this procedure employed. The former drug does not affect the motor fibers of the mixed nerves to the same extent that the latter does and therefore does not produce sudden paralysis of the respiratory muscles and temporary respiratory distress as does the latter drug. In thoracic wounds with the pleural cavity wide open I repeatedly used high spinal procaine hydrochloride anesthesia in order to avoid cough.

and deep inspiratory and expiratory movements provoked by inhalation anesthetics, during the induction period, the disastrous effect of which on the heart, is well known. I have had gratifying results with this method. The site of the injection, the fifth dorsal space, is not to my mind an argument against the procedure. The anesthetic is readily fixed in the posterior roots and has no tendency to go upward. Syncope is due, when it occurs, to cerebral anemia secondary to the extreme abdominal vasodilatation from paralysis of the splanchnic nerves. The patient "bleeds into his own vessels." No direct action of procaine hydrochloride, with the small dosage employed, on the centers of the fourth ventricle has so far been proved. I rather believe that deaths from spinal anesthesia are due either to the use of excessive amounts of the anesthetic or to a failure to put the patient in a slight Trendelenburg position, which insures a sufficient amount of blood both to the brain and to the territory of the vena cava, so that notwithstanding the extreme abdominal vasodilatation, enough blood comes back to the right side of the heart to insure its functioning. It is therefore less dangerous to use smaller quantities of procaine hydrochloride and inject these into the space corresponding to the metameres to be anesthetized, than to inject the anesthetic into the "safer" low spaces and use two or three times these amounts.

A last point of interest, which has already been emphasized, is the quiet respiration and undisturbed circulation despite the wide opening of the pleural cavity—which is due to the preliminary collapse of the lung. I wish to emphasize this point again because, knowing it, one operates without fear of a precipitous catastrophe and without the hindrance of a limited exposure of the operative field, this insures smoothness, speed and accuracy—indispensable factors in the success of an intrathoracic operation.

The second case pictures the postpneumonic and postempyemic type of bronchiectasis. Protracted pneumonia with the persistence of a focus of consolidation (due, to my mind, to persistent bronchial obstruction) is the determining cause of this form of bronchiectasis. Empyema does not clear up after thoracotomy because of the persistence of the infection in the underlying lung and the bronchial fistula. Repeated operations do not clear the condition because they do not strike at the cause. The existence of a more or less voluminous pleuropulmonary cavitation communicating with an internal bronchial fistula is misleading. Not until the bronchial dilatations and multiple small abscesses due to diffuse bronchopneumonitis secondary to bronchial obstruction are cleared up, can cure follow. The clinical symptoms improve when the "honey-comb" lesion is more or less sufficiently drained through a tube penetrating one of these cavities and proportionately to the extent that this

one cavity communicates with the others. The symptoms reappear whenever this drainage fails. In the meantime the disease spreads over the lung while the surgeon wonders why the patient does not improve, although "the cavity is adequately drained." An intrabronchial injection of iodized oil solves the problem by showing the existence of bronchiectatic lesions. Only an eradication of the involved parenchyma in the chronic cases (and even then often only with the help of a permanent bronchostomy) insures a clinical cure. Bronchoscopic treatment in the early stages of the disease in this case would possibly have cleared up the affected pulmonary area. I agree with Pickhardt in considering "delayed pneumonias" cases calling for an active and early surgical treatment. When the disease has advanced, procrastination and "transference" of the unfortunate patients with the discharge note "improved" will certainly not cure them. They are doomed to certain death. Is it not better to take the only chance which is a radical operation? Sauerbruch, Lilienthal, Meyer, Torek and their followers took these chances and have saved more lives than have the conservatives in this field. As against such conservatism, I would advocate a very conservative boldness. Only by perfecting operative procedures and decreasing the associated mortality will a solution of the problems of bronchiectasis be found. This goal can be attained by a more extensive study of the physiology of these morbid states and it is on this ground that I have submitted these suggestions.

# CONCLUSIONS

1. A clinical classification distinguishing different forms of bronchiectasis is suggested, and the practical usefulness of these distinctions has been set forth.

2. The necessity for using a prolonged and progressive treatment against a chronic and progressive disease is shown.

3. In advanced forms of bronchiectasis, only eradication of the diseased parenchyma of the lung can produce a cure. This, according to the case, should be done by resection (lobectomy), cauterization (cautery pneumectomy of Graham) or exteriorization (Whittemore).

4. In order to decrease the mortality incident to these operative procedures, a technic of "multiple stage lobectomy" is outlined in which the following stages are systematically performed in the order named: artificial pneumothorax, phrenicectomy, thoracoplasty and lobectomy.

5. In support of this method, physiologic, pathologic and clinical data have been presented.

6. Two cases of advanced bronchiectasis in which cure was achieved by the use of this technic are reported.



# COMPARATIVE VALUE OF SPLANCHNIC AND SPINAL ANALGESIA IN THE TREATMENT OF EXPERIMENTAL ILEUS\*

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About fifteen months ago, we had occasion to make a preliminary report of results obtained in the treatment for experimental ileus by the induction of splanchnic analgesia. In that communication we expressed the opinion that splanchnic analgesia was preferable to spinal analgesia, at least from the point of view of safety to the patient. From the theoretical point of view spinal analgesia and splanchnic analgesia accomplish the same end in that they both produce a block of the splanchnic nerves. In one case (spinal analgesia) the block in the reflex pathway is made at the point of emergence of the white ram communicantes from the spinal cord, while in the other (splanchnic analgesia) the splanchnic nerves are blocked only after their complete formation as they lie in the retroperitoneal tissues anterior to the bodies of the last dorsal and first and second lumbar vertebrae. Other things being equal, chemical section of the roots entering into the formation of the splanchnic nerves, by means of spinal analgesia, should be as effective as chemical section of the nerves produced by infiltration further on in their course. At the time of our previous investigation we were not in possession of any facts indicating the relative efficiency of the two methods that are available for the production of a splanchnic block.

## ANATOMIC AND PHYSIOLOGIC CONSIDERATIONS

In order to gain a lucid conception of what splanchnic block may be expected to accomplish with respect to restoration of motor function to a paralyzed loop of intestine, it becomes necessary to review briefly the nervous regulation of the intestinal movements. As has been appreciated from the early beginnings of physiology, the intestine is capable of normal motor activity in the absence of all extrinsic nerve control. There is some evidence, however, that the rhythmic or pendular activity of the intestinal tube is closely dependent on the nerve elements which

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enter into the formation of the so-called plexuses of Auerbach and Meissner. That the orderly, rhythmical movements of the intestine are dependent on its intrinsic nervous system, and not on any inherent power possessed by the individual muscle cell, is accepted by some observers but denied by others. Rosenstein and Kohler<sup>1</sup> stated that if the mucosa and submucosa are removed from a loop of intestine the automaticity of the intestinal movement in the affected loop is not disturbed. Since the plexus of Meissner lies within the submucosa just beneath the mucosa, and the procedure of removing the submucosa detaches this plexus from the underlying musculature, it is to be presumed that the plexus of Meissner is little or not at all concerned with the intrinsic movements of the intestine. According to Rosenstein and Kohler, however, separation of the circular from the longitudinal layers of the muscular coat of the intestines destroys the automatic activity of the circular fibers, but does not affect the automaticity of the longitudinal fibers. Gunn and Underhill,<sup>2</sup> Alvarez and Mahoney,<sup>3</sup> and von Esoeld<sup>4</sup> were not in agreement with this view of the intrinsic nerve regulation of the intestine, since they found that the circular muscular layer when deprived of its associated nerve net continues to show the function of automatic rhythmicity.

The extrinsic, or regulatory, nerve supply to the intestine is derived partly from the vagi and partly from the splanchnic nerves. Gaskell,<sup>5</sup> Macleod,<sup>6</sup> Bayliss and Starling,<sup>7</sup> and others have presented evidence to show that the primary action of the vagi is motor, while the action of the splanchnic nerves is essentially antagonistic and performs the function of inhibition. Bayliss and Starling<sup>7</sup> have shown that stimulation of the vagi causes a preliminary inhibition but Hotz<sup>8</sup> made the observation that the stimulation of any sensory nerve produces an

1 Rosenstein P. and Kohler, Hans. Ueber die Beeinflussung der Darmparalyse durch Nikotininjektion in das Ganglion Coeliacum. *Deutsche Ztschr. f. Chir.* **210** 315, 1928.

2 Gunn, J. A., and Underhill S. W. F. Experiments upon the Survival of Mamalian Intestine, *Quart. J. Exper. Med.* **8** 275 1914.

3 Alvarez, W. C., and Mahoney, L. J. Myogenic Nature of Rhythmic Contractions of Intestine, *Am. J. Physiol.* **59** 421, 1922.

4 Von Esoeld, L. W. Verhalten von plexushaltigen und plexusfreien Darmmuskelpreparaten, *Arch. f. exper. Path. u. Pharmacol.* **134** 357 1928.

5 Gaskell W. H. *The Involuntary Nervous System*. New York: Longmans Green & Company, 1916.

6 Macleod J. J. R. *Physiology and Biochemistry in Modern Medicine*. S. Louis: C. V. Mosby Company, 1922.

7 Bayliss W. B. and Starling E. H. Preliminary Note on the Innervation of Small Intestine, *Proc. Physiol. Soc. Lond.* **24** 122 1889.

8 Hotz, Gerhard. Beiträge zur Pathologie der Darmbewegungen. *Mitt. u. Grenzgeb. d. med. u. Chir.* **20** 257 1909.

initial inhibition of intestinal movement Since the vagi contain a certain number of sensory fibers, preliminary inhibition, as a result of stimulation of these nerves, is to be expected Hotz<sup>8</sup> expressed the belief that inhibition is produced by way of the splanchnic nerves, since he found that mechanical section of these nerves produces augmentation of intestinal movements Stimulation of the splanchnic nerves produces an initial inhibition presumably due to the fact that they contain sensory fibers, but increased motility ensues thereafter, and this effect is both pronounced and prolonged, indicating that the essential function of the nerve is one of inhibition

Our experimental results have been fully in accord with the views expressed by the foregoing authors We have repeatedly and invariably

Fig 1—Kymographic tracing, showing normal intestinal movement, blood pressure readings and respiration The left vagus nerve was stimulated by means of a faradic current at the point shown by the arrow This produced a temporary cessation of the heart beat as shown in the upper curve A temporary cessation in intestinal movement also occurred, however, with an increase in intestinal tone In this particular instance, following the return of intestinal tone to normal, intestinal movement was resumed, and after about thirty seconds became more active than before

found that stimulation either of the right or of the left vagus nerve in the neck, whether by mechanical or by electrical means, produces a definite increase in the amplitude of intestinal movements This effect, however, is characteristically seen only after an initial period of inhibition, which lasts for a varying period of time, but usually for only one minute or less An initial increase in tone of considerable magnitude is characteristically seen in the intestine within from five to ten seconds after stimulation This phase, however, is also only transitory (figs 1 and 2) The initial increase in tone and the subsequent short

period of inhibition of intestinal movement as previously described and as shown in figures 1 and 2, are not peculiar to stimulation of the vagus nerve as such, but occur whenever sensory nerves in any part of the body are stimulated. Thus the introduction of the point of a needle during splanchnic analgesia, any dissection, as, for instance, the isolation of a blood vessel, or any pinching or squeezing, as during the course of the application of a hemostatic forceps, produces an exactly similar effect. For this reason we must assume, with Hotz that the preliminary inhibitory phase of vagus stimulation is the result of an action on the sensory fibers rather than on the motor fibers of which the vagus nerve is composed. Conversely cutting of the vagi

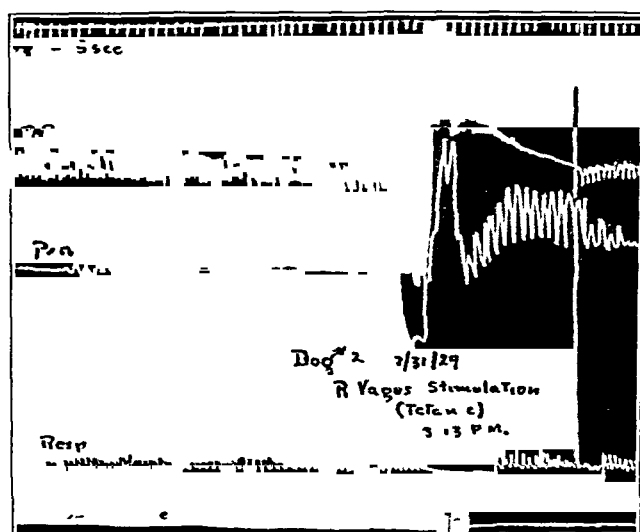


Fig 2—Kymographic tracing, showing the effect produced by stimulation of the right vagus nerve with a faradic current. Immediately following this stimulation there was a cessation of intestinal movement, associated with a definite increase in intestinal tone. After the return of intestinal tone to normal, the intestinal movement became much more active than before stimulation.

has been found to produce a decrease in the amplitude of intestinal movements, preceded, however, by a transitory increase in motility which presumably results from the transitory mechanical stimulation incident to the section. Moderate decrease in motility is noted after the section of one vagus nerve, but when both vagi are cut the effect is still more noticeable (fig 3). This diminution of intestinal movement lasts for a variable period of time, after which the intestine tends to resume its normal motility, the nerve motor-inhibitor mechanism apparently being capable of readjusting itself with a fair degree of rapidity following the loss of either one or the other of its two antagonistic sets of regulatory nerves.

Stimulation of either the right or the left greater splanchnic nerve tends to produce a cessation of intestinal movement and loss of tone. In favorable cases intestinal movement can be made to cease almost entirely (figs 4 and 5). Although the inhibitory effect of such stimulation is definite, as shown in figures 4 and 5, it represents stimulation of the greater splanchnic nerve only, the lesser splanchnic nerve being exceedingly difficult to isolate because of its anatomic relations.

Cutting of the greater splanchnic nerves is followed by a definite increase in tone and an amplitude of intestinal movements, as shown in figure 6.

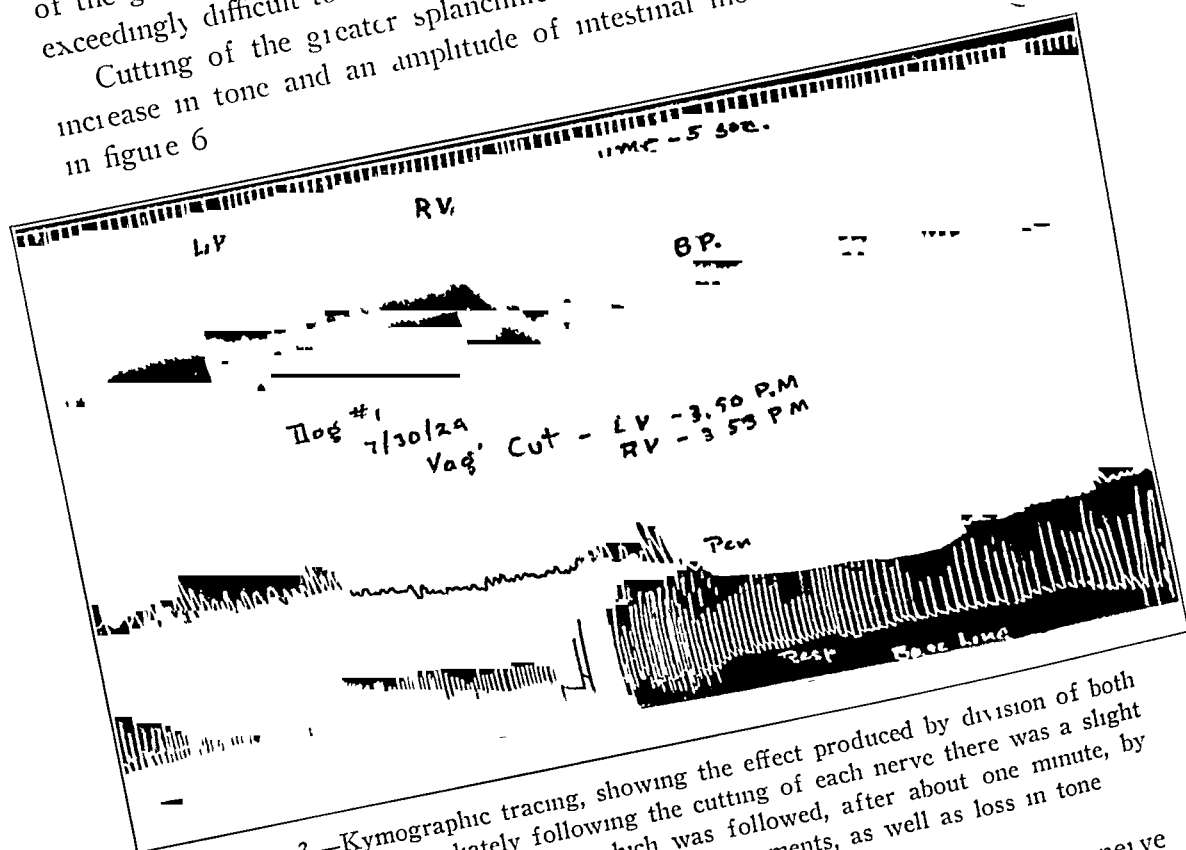


Fig 3—Kymographic tracing, showing the effect produced by division of both vagus nerves. Immediately following the cutting of each nerve there was a slight increase in intestinal movement, which was followed, after about one minute, by almost complete cessation of all intestinal movements, as well as loss in tone.

Following division of either the vagus or the sympathetic nerve supply, the effect of stimulation of the antagonistic pair of nerves shows a highly exaggerated effect. Thus, after section of the splanchnic nerves, stimulation of the vagi produces an unusually marked increase in amplitude of intestinal movements (fig 7), and stimulation of the splanchnic nerves, after vagotomy, tends to produce relatively profound inhibition.

Theoretically, any therapeutic measure aimed at the restitution of motor activity to a paralyzed intestine might take as its point of departure (1) the muscle cell itself, (2) the intrinsic nervous system of the intestine (plexuses of Auerbach and Meissner) or (3) the

extrinsic nerve supply, viz, the vagus nerves and the splanchnic nerves. Considering only the extrinsic nerve supply any attack directed against the vagi must of necessity involve stimulation, whereas a similar attack directed against the splanchnic nerves must involve paralysis

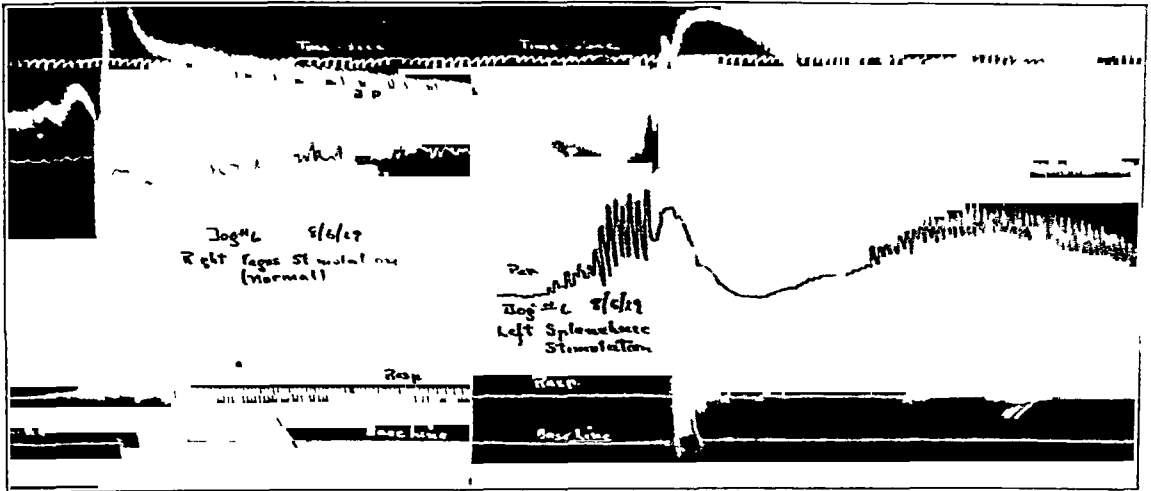


Fig 4—Kymographic tracing showing the effect of stimulation of the left greater splanchnic nerve on blood pressure and intestinal movement. As indicated by the arrow the left splanchnic nerve was stimulated with a faradic current when intestinal movement was active. This produced an immediate rise in blood pressure which returned to normal after about two minutes. There was an immediate cessation of all intestinal movement and a temporary increase in intestinal tone followed by a marked loss of tone.

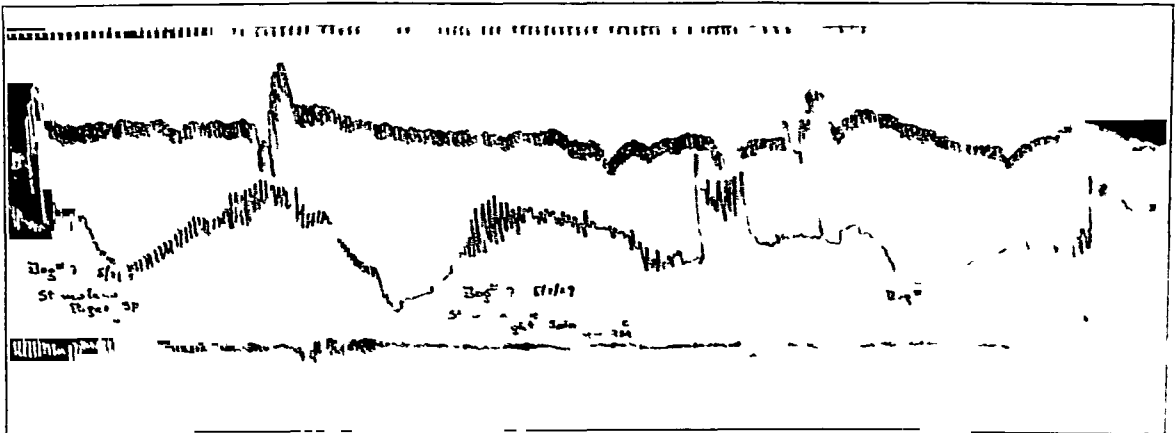


Fig 5—Kymographic tracing showing the effect of stimulation of the greater splanchnic nerves on blood pressure, intestinal movement and intestinal tone. The tracing shows three successive stimulations of the right greater splanchnic nerve. A repetition of effect results in a momentary rise in blood pressure, an immediate cessation of all intestinal movements and a loss of intestinal tone.

Interruption of impulses traveling centrifugally along the splanchnic nerves may conveniently be performed in two places by chemical means the first, at the point where the white rami communicantes leave the spinal cord by way of the ventral or motor root, the second, in the retro-peritoneal space in the region of the first lumbar vertebra, where the nerves enter into the formation of the semilunar ganglia and the greater, lesser and least splanchnic plexuses. Chemical section of the roots entering into the formation of the splanchnic nerves is technically not difficult, since it involves merely the introduction of an anesthetic solution sufficiently high into the subarachnoid space to anesthetize the segments of the cord from the fifth dorsal to the first

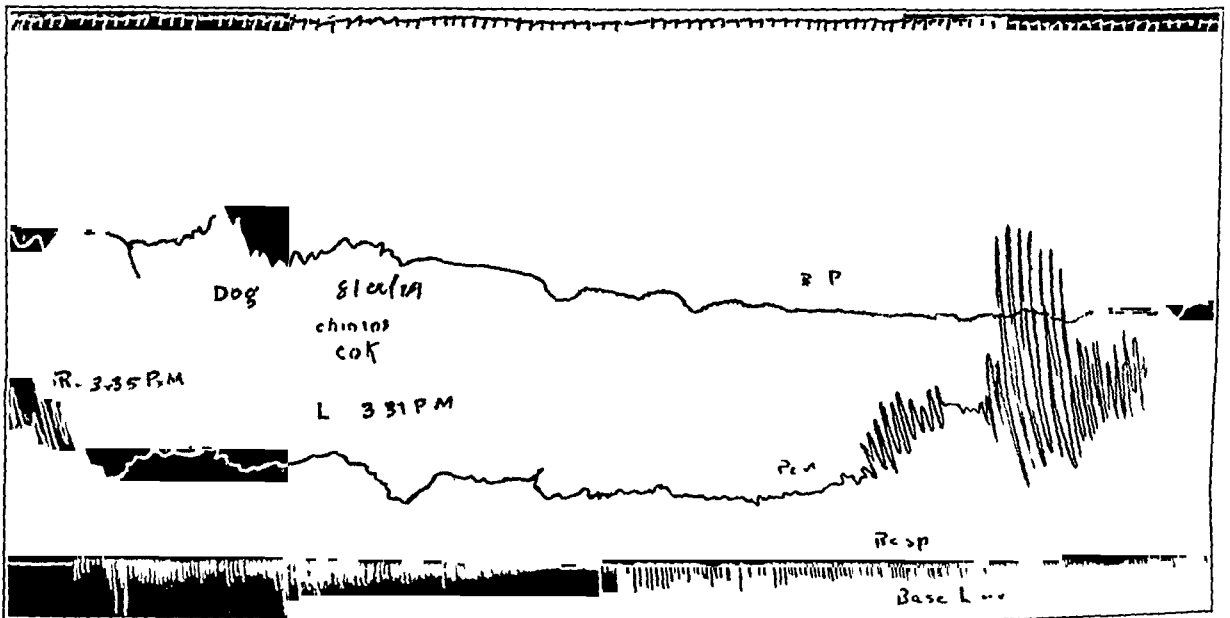


Fig 6—Kymographic tracing, showing the effect produced by division of the splanchnic nerves. At the point marked by *R*, the right splanchnic nerve was divided, and at the point indicated by *L* the left splanchnic nerve was divided. Following division of the right splanchnic nerve intestinal movement, which had been active previously, became almost completely abolished. About three minutes after division of the left splanchnic nerve, the intestinal movements became hyperactive. The tone of the intestinal muscle becomes markedly increased. There is also a definite decrease in the blood pressure, which is gradual.

lumbar vertebra. Such a procedure is, of course, commonly employed in operations on the organs lying in the upper part of the abdomen. Actually the performance of spinal analgesia is not without danger, not only from the point of view of infection, to which the leptomeninges are particularly susceptible, but also from the point of view of intradural hematoma formation and mechanical injury to the cord, which could occur, of course, only in those cases in which puncture is made at a higher level than the termination of the cord, although in this con-

nection the considerable variation in the level of the position of the conus medullaris must be remembered. With respect to the level attained as a result of spinal analgesia, it must be borne in mind that an anesthetic solution once introduced into the dural sac cannot be removed and the height which anesthesia may attain is, therefore, only partly within the control of the anesthetist.

Splanchnic analgesia by the posterior route, that is, according to the technic of Kappis<sup>9</sup> although technically a somewhat more formidable procedure than that of spinal analgesia, is relatively devoid of danger when carefully performed and for this reason seems a more logical

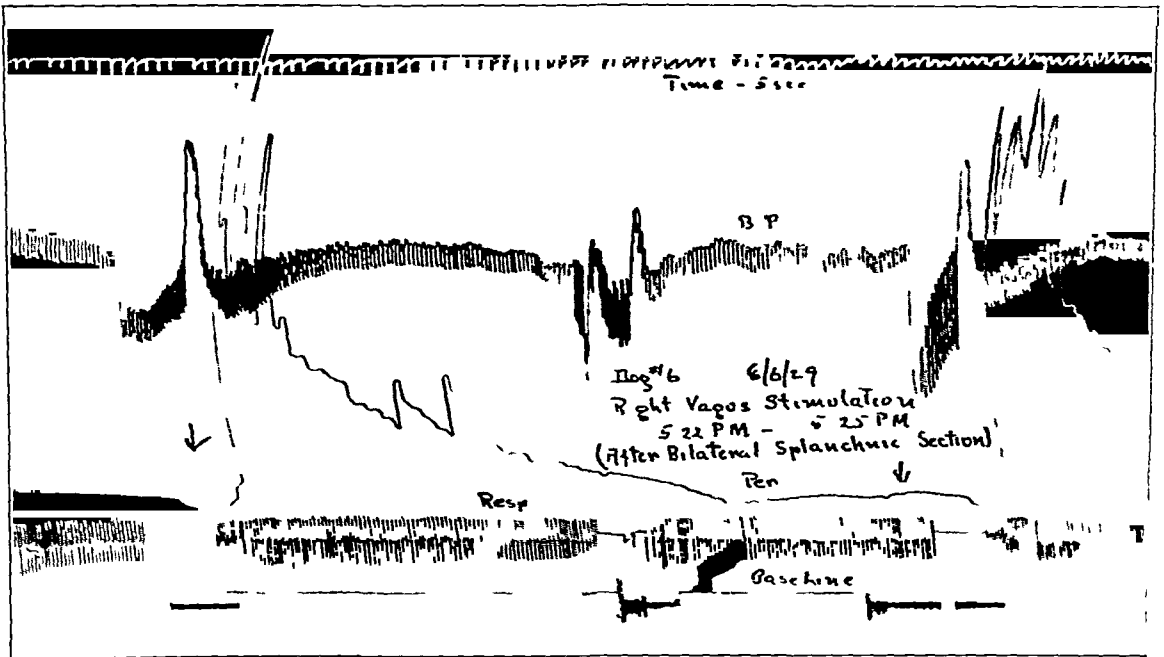


Fig 7—Kymographic tracing, showing the effect of vagus stimulation on intestinal movement after bilateral splanchnic section. At the point indicated by the first arrow, the right vagus was stimulated by a faradic current. Immediately following each stimulation there was a marked increase in intestinal tone, as well as intestinal movement, no movements having been noted previous to these stimulations.

procedure. Of the drugs used in producing spinal analgesia, only those having a local anesthetic action are suitable. When the method of splanchnic analgesia is used, however, not only anesthetic substances but any drug which is capable of interfering with the transmission of impulses through the sympathetic ganglia may be used for example

<sup>9</sup> Kappis, M. Erfahrungen mit Lokalanesthetie bei Bauchoperationen. Verhandl d deutsch Gesellsch f Chir 43:87, 1914.



nicotine, which presumably exerts no effect on the nerve trunk itself, but paralyzes the synaptic junction in the semilunar ganglia

The present report concerns particularly a consideration of the relative merits of spinal and splanchnic analgesia, and, as far as splanchnic analgesia is concerned, with the relative merits of the drugs procaine hydrochloride and nicotine. The experimental results reported were obtained from a series of seventy dogs. Most of these animals were rendered anesthetic prior to operative manipulation by the introduction of from 0.18 to 0.3 Gm. of sodium barbital per kilogram of body weight through a stomach tube, but in several animals ether anesthesia was used. All the experimental data have been recorded by kymographic tracings, and are, therefore, we believe, of far greater value than deductions from unaided ocular observations, however carefully the latter may be made. The operative technic consisted of laparotomy, followed by the introduction, through a small incision in the intestine, of a thin walled, rubber balloon into the lumen of the intestine, the balloon being connected by means of a small rubber tube to a "Marey tambour" arranged to record, by means of a lever and writing point, on a lightly smoked kymographic drum. In every case concomitant blood pressure tracings were obtained from the carotid artery by means of cannularization, pressure variations being conducted through a system of rubber tubes filled with sodium citrate solution to a mercury manometer, which, in turn, was provided with a "ridei" and a recording point. Respirations were also recorded by means of a recording point, actuated by a tambour and connected by a rubber tube to a tracheal cannula. In almost all the cases the vagi were dissected free during the course of the operative manipulation incidental to the insertion of the carotid and tracheal cannulas. In certain cases in which the splanchnic nerves were isolated, the operative approach was through the flank in the region of the costovertebral angle, and access was thereby gained to the retroperitoneal space without perforation of the posterior parietal peritoneum. For the most part, the operative procedures incident to the opening of the abdomen and the placing of balloons within the lumen of the intestines were performed in a bath of warm saline solution. In this manner, the peritoneum and the contents of the peritoneal cavity were protected from exposure to the air and chilling.

#### SPLANCHNIC ANALGESIA (NICOTINE)

Because of the beneficial effects of spinal analgesia in the treatment for ileus observed by others, Rosenstein and Kohler<sup>10</sup> conceived the

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10 Rosenstein, P., and Kohler, Hans. *Therapeutische Versuche zur Bekämpfung der Darmlamung durch Umspritzung des Ganglion Coelicum*, *Med. Klin.* 22: 530, 1926.

idea that if the splanchnic nerves were blocked by some substance which would be specific for these nerves, patients with ileus might be even more effectively treated. Because nicotine is supposedly specific in its action on sympathetic ganglia, its action being that of paralysis of the synaptic junctions, these investigators employed this drug both experimentally and clinically. They reported their results on twenty-two normal rabbits. In this group of animals and in six additional rabbits in which peritonitis had previously been produced by the injection of pure cultures of streptococci they injected various drugs into the region of the celiac ganglia but among these drugs nicotine was conspicuous by its absence. These particular experiments are described by Rosenstein and Kohler<sup>1</sup> in great detail. The experiments that they supposedly performed with nicotine are mentioned only briefly and are not described in detail, they stated merely that the results obtained by the injection of nicotine into the splanchnic area are "similar" to those obtained by the injection of other substances including procaine hydrochloride. Rosenstein and Kohler reported twenty-six clinical cases of ileus in which the patients were treated by the injection of nicotine "into the celiac ganglia." Seventeen of the twenty-six patients were relieved of their ileus, nine, however, subsequently died. These authors expressed the opinion that in nine cases, in which no increase in peristaltic activity was obtained an inactive nicotine salt had been injected.

In order to verify the results obtained by Rosenstein and Kohler,<sup>1</sup> the following experiments were performed. In nine dogs, a nicotine solution was injected into the splanchnic area. In two animals two injections were made. In all cases a balloon was inserted, as previously described, into the duodenum, ileum, and colon, respectively. In eight of the nine animals, the nicotine solution was injected into the splanchnic area, according to the technic of Kappis, within a short time after the stimulation of the vagi with the faradic current. The ninth animal had received two prior injections of procaine hydrochloride into the splanchnic area before the nicotine solution was injected. The results obtained in the latter case, however, correspond with the general results obtained in the other cases. The effect produced by the introduction of a nicotine solution into the splanchnic area was as follows. There was a marked and constant increase in blood pressure which with the exception of three instances, was always greater than 90 mm of mercury. This blood pressure effect was transitory however lasting not more than three minutes the pressure thereafter returning to or falling slightly below normal (figs 8 and 9). The amount of nicotine administered was always 1 minim (0.06 cc) (except in three instances), since this amount was the utmost that was considered safe to give. In

one case in which 0.5 minims (0.03 cc) was given, there was a blood pressure increase of only 10 mm of mercury. In one case in which 10 minims (0.60 cc) was given, there was an increase of considerably more than 154 mm of mercury (the utmost capacity of the manometer), the rise in pressure being so rapid and great that the mercury was forcibly ejected from the free arm of the manometer. A third animal showed no remarkable effect from the injection of 2 minims (0.12 cc) of nicotine in divided doses. In each instance the given amount of nicotine was diluted with 20 cc of distilled water, 10 cc of this solution being injected on either side into the splanchnic area. This corresponds to the technic employed in splanchnic analgesia obtained with procaine hydrochloride in which relatively large amounts of fluids must be used.

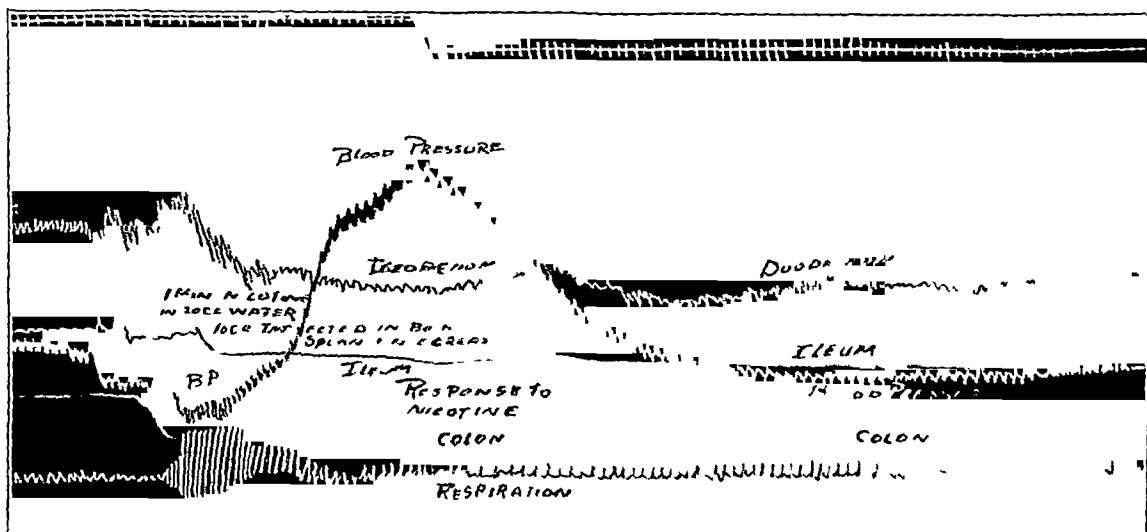


Fig 8—Kymographic tracing showing the effect on blood pressure and intestinal movement of the introduction of nicotine into the splanchnic area. The most marked effect was a progressive and marked rise in blood pressure, the blood pressure fell to normal about three minutes after having reached its greatest height. There was a marked increase in respiration which temporarily increased the pressure in the duodenum, the intestinal tracing was complicated by a superimposed respiratory component. There was a decrease in tone in the ileum, and six minutes after the administration of the nicotine a definite but temporary increase in intestinal movement was noted.

to allow for unavoidable variations in the position of the point of the needle, through which the solution is injected. Owing to the depth of the injection, it is obviously impossible to direct the point of the needle accurately into the ganglion itself. The best that can be anticipated is a deposition of the solution somewhere in the immediate vicinity of the ganglion. Rosenstein and Kohler,<sup>1</sup> in their experimental work on rabbits, injected the nicotine solution directly into the celiac ganglion

through a laparotomy incision after complete evisceration of the abdominal contents a procedure which is obviously impossible in the clinical treatment of the average patient with ileus. When splanchnic analgesia is performed clinically with nicotine these investigators advocate a modification of the original Kappis technic in that the point of the needle is thrust several millimeters beyond the ventrolateral surface of the body of the vertebra. Such a procedure is distinctly dangerous because of the likelihood of wounding the inferior vena cava or aorta. These authors stated that it is not only possible but necessary to inject the nicotine solution directly into the ganglion a procedure which is obviously chimerical.

In our series of experiments the effect on the duodenum, ileum and colon produced by the introduction of the nicotine solution into the splanchnic area was inconstant with respect to both changes in the intestinal tone and the amplitude of intestinal movements. In five cases

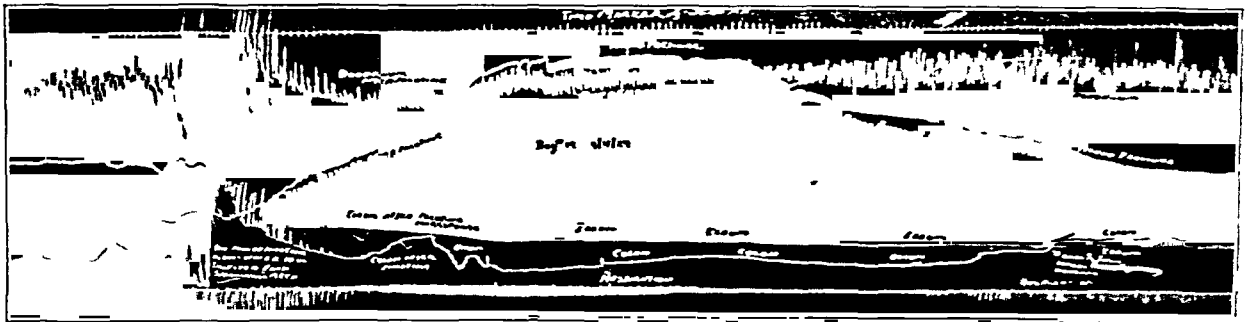


Fig 9—Kymographic tracing, showing the effect produced by the introduction of nicotine into the splanchnic area. As shown by the lowermost tracing a definite increase in respiratory movement resulted. The duodenal tracing, which is the second from the top, was complicated by a superimposed respiratory component. The blood pressure tracing showed a typical gradual progressive rise, which reached a maximum after about four minutes, remained elevated for two and one-half minutes and returned gradually to normal. There was no change in either intestinal movement or tone in the ileum. The colon however, showed a slight increase in tone.

the tone of the ileum was increased between 10 and 50 mm. In only one case did the colon show any increase in tone (20 mm). In all the other cases in which a change was noted it was in the direction of a decrease, which in no case was greater and usually was considerably less than 15 mm. With respect to the effect of peristaltic movements on amplitude, negligible effects were usually seen. In one case however, an increase of 10 mm was noted in the ileum and in another case a decrease of 10 mm in the colon. Otherwise changes varied from 1 to 3 mm.

From these results we are forced to conclude that nicotine when injected into the splanchnic area is probably of little or no value in the treatment for ileus. It is conceivable that the injection of nicotine directly into the semilunar ganglion might produce more pronounced effects than we have been able to obtain by diffusion of the solution. However, diffusion is the only method that is clinically available and safe. Furthermore, the injection of nicotine is open to serious objections in that it produces rapid and exaggerated increases in blood pressure. While this hypertension might be tolerated with impunity by young persons and those with normal vascular systems, it might prove disastrous to patients with an abnormally high blood pressure and especially to those with vascular lesions.

#### SPLANCHNIC ANALGESIA (PROCAINE HYDROCHLORIDE)

Our experimental experience with splanchnic analgesia obtained with procaine hydrochloride now extends over a series of fifty animals. Splanchnic analgesia has been induced in all cases by the posterior route, according to the technic of Kappis.<sup>9</sup> In the experiments reported in a previous contribution,<sup>11</sup> all of the observations were made on animals having experimentally produced intestinal obstruction. The present series of experiments includes normal animals and also ones in which mechanical obstruction had been present for varying lengths of time. In our previous investigation tracings were obtained from the ileum alone. In the present series tracings were obtained of movements in the duodenum, ileum and colon in a number of animals, the three balloons being used coincidentally.

Although the technic of the introduction of procaine hydrochloride solution for the production of splanchnic analgesia has been the same in all of our experimental investigations, the quantity of solution so introduced and the strength of the solution have varied somewhat. Our original observations were made, for the most part, on animals that had received 20 cc. of a 1 per cent solution of procaine hydrochloride bilaterally. In subsequent cases, we have most frequently used 10 cc. of a 2 per cent solution of procaine hydrochloride bilaterally. In a few instances, as little as 5 cc. on either side has been used.

In general, following the induction of splanchnic analgesia by procaine hydrochloride similar changes in intestinal motility and tone are noted in both normal and obstructed animals. The obstructed animals show a distinct tendency to react more actively than the normal ones. Much more constant and noteworthy effects are shown by the intestines of the animals in which only one balloon has been introduced. How-

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<sup>11</sup> Ochsner, A., Gage, I. M. and Cutting, R. A. Treatment of Ileus by Splanchnic Anesthesia. *J. A. M. A.* **90** 1847 (June 9) 1928.

ever, animals into whose intestinal canals three balloons have been introduced show unmistakably similar motor effects. This observation is interpreted as evidencing the inhibitory effect produced by trauma on intestinal movements, since the operative manipulation required to introduce the three balloons represents not only the trauma of three enterostomies, but also such injury as must inevitably be inflicted during the course of traction on the mesentery and surrounding structures incident to the isolation and identification of the various parts of the intestinal tract on which enterostomy is to be performed. Motor effects on the intestines of both normal and experimentally obstructed animals included not only a rise in the tone of the intestine which in most cases was considerable, but also a somewhat spectacular increase in intestinal movements (figs 10 and 11). In a certain number of cases, splanchnic

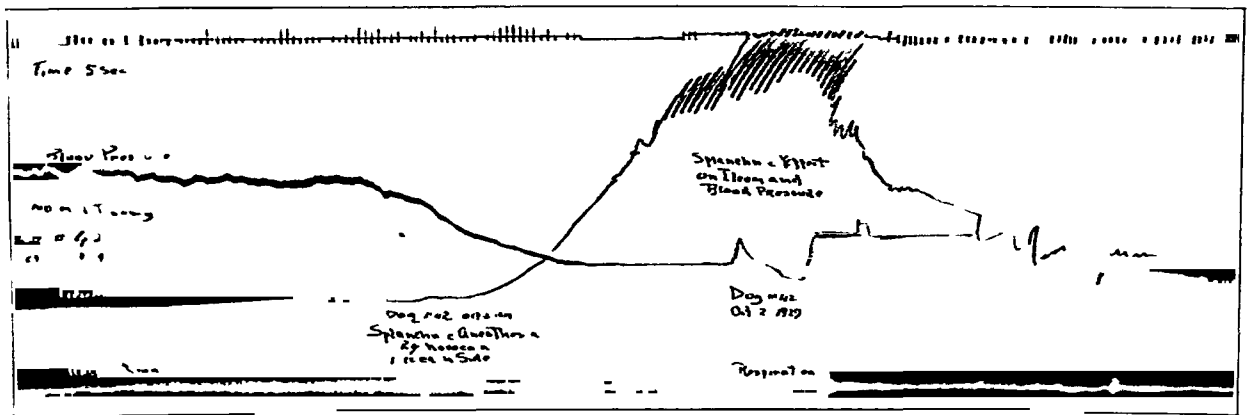


Fig 10—Kymographic tracing, showing the effect produced by splanchnic block with procaine hydrochloride. Following the production of splanchnic analgesia, there was a typical decrease in blood pressure, which was followed after one and one-half minutes by a marked increase in intestinal tone, and this in turn was followed, after an additional minute, by a definite increase in intestinal movements. The increase in intestinal tone was only temporary, lasting about three minutes. The increase in intestinal movements, however, persisted.

analgesia has been unsuccessful in restoring motility to a paralyzed intestinal musculature. Failures, when encountered, have usually been due to lapses in technic in the injection of the anesthetic solution. This has been evidenced by the fact that the blood pressure has remained unaffected. Splanchnic effects have never been noted in the absence of blood pressure changes. In a few cases although the blood pressure has shown characteristic diminution the motor activity of the intestine has been unaffected. In no case in which splanchnic analgesia has failed to produce characteristic motor effects in the intestine, however, has any other maneuver which we have been able to employ been suc-

cessful in restoring motor activity. This is equivalent to saying that splanchnic analgesia has been the most successful agent in the production of intestinal movements that we have been able to employ.

Because of the mechanical features that we have used in recording intestinal activity, actual measurements are of merely relative value, since the size of the balloon used in the lumen of the intestine, as well as the leverage applied to the writing point on the kymographic drum, has been subject to minor variations, over which the experimenters have had incomplete control. In eight animals in which the ileal tracings alone were attempted, a constant rise was recorded in the tone of the intestine, with the single exception of one animal, in which both splanchnic nerves had previously been cut, which animal, therefore, presented an excellent control for the other experiments. The average increase in tone on the kymographic tracing was 29.5 mm. As previously stated, the latter figure is of only relative significance, but the evaluation of the figure may perhaps be appreciated when it is

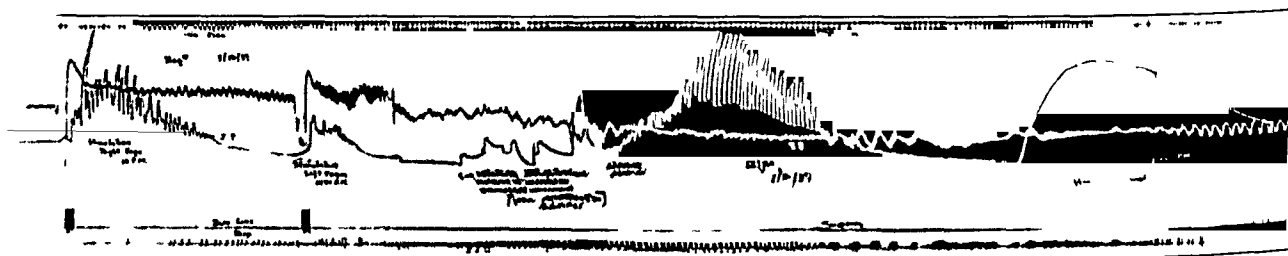


Fig. 11—Kymographic tracing, showing the effect of vagus stimulation and splanchnic analgesia. At the extreme left of the tracing a typical reaction in both the ileum and the blood pressure was produced by stimulation first of the right and then of the left vagus nerves by means of a faradic current. In the center of the tracing the animal was turned and a splanchnic analgesia was produced. There followed a slight fall in blood pressure, which, however, was not marked. After about one and one-half minutes there was an increase in intestinal movement, followed by a marked increase in intestinal tone. This increase in tone lasted about one and one-half minutes, at which time the tone became greatest. The tone then fell for an additional two minutes, and reached its lowest level at the end of this period. Intestinal movement persisted for an additional two minutes. Three and one-half minutes after the tone of the intestine had assumed a normal level, the tone again increased remarkably without, however, any evident increase in intestinal movement. This increase in tone is similar to that observed in the first instance.

realized that with the use of the same system and the same application of leverage the normal amplitude of intestinal movement was represented by an excursion of the lever which was not ordinarily greater than from 3 to 4 mm. In addition to this rather spectacular increase in tone, the amplitude of intestinal movement itself is invariably increased after the production of a successful posterior splanchnic anal-

gesia In these eight animals, the average increase in the amplitude of movement, as recorded on the drum, was 11.2 mm

As to the average duration of the effect of posterior splanchnic analgesia obtained with procaine hydrochloride, the increase of tonus is considerably more transitory than the increase of intestinal movement The total duration of the motor effect of posterior splanchnic analgesia varies considerably It has ordinarily been not less than from five and one-half to six minutes, and occasionally has been seen to persist for as long as one-half hour or more The duration of the spectacular rise in tonus ordinarily lasts for only from three to four minutes, although occasionally somewhat longer Although the motor effect of posterior splanchnic analgesia on the intestinal motility is never noted in the absence of diminution in blood pressure, there seems to be no constant relationship between the amount of the blood pressure effect and the magnitude of the changes in intestinal tonus and movement Sometimes animals showing rather insignificant decreases in blood pressure manifest spectacular changes in intestinal tone and motility while animals showing radical decreases of blood pressure may show rather insignificant motor and tonus changes On an average, the amount of decrease of blood pressure noted in our experimental dogs has been 20 mm of mercury However, characteristic motor and tonus changes have been noted in animals showing a decrease in blood pressure of only 2 or 3 mm, while certain animals have shown decreases of from 50 to 56 mm of mercury

When the effects of posterior splanchnic analgesia produced by procaine hydrochloride on the duodenum, ileum and colon, as shown in those animals in which balloons were introduced coincidentally into different parts of the intestinal tract are compared, the effect on the ileum is much more striking than the effect on either the duodenum or the colon No changes of significance have been noted in the colon in respect to either tonus or motility This observation is not inconsistent with what is known concerning the innervation of the colon The splanchnic analgesia discussed in these experiments is not calculated to interfere with the splanchnic fibers that supply the lowermost part of the intestinal tract In fact, it is doubtful that colonic movements are under the same sort of dual innervation as the more cephalad portion of the gut It has been stated that the splanchnic fibers supplying the colon act in both a motor and a sensory capacity According to Langdon Brown,<sup>12</sup> however, the nerve supply of the large bowel is derived from the pelvic visceral nerve and the inferior mesenteric ganglion, the former being motor the latter inhibitory

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12 Brown, Langdon. *The Sympathetic Nervous System in Disease*. London: Henry Troude and Hodden and Houghton, 1923.



The effect of splanchnic analgesia on the duodenum is considerably more variable than is the effect on the ileum. As previously stated, when the "three balloon technic" was used, the results of splanchnic analgesia were relatively inconstant, but this inconstancy was noted particularly in the duodenum as compared with the ileum. As a rule, increases in duodenal tone and movement apparently are caused by splanchnic analgesia obtained with procaine hydrochloride. In some cases increases in tone have been very great. In one case this amounted to 40 mm, but usually the increase was not greater than 5 mm. These values, like the values given previously in the discussion of the effects on the ileum, are of only relative significance, but the balloon, the connection and the system of levers were purposely made as similar as possible in all cases, so that a fall or a rise of a given number of millimeters in the duodenum can be compared fairly with a similar rise or fall in either the ileum or the colon. In some instances, the effect of splanchnic analgesia on the duodenum apparently was expressed in a decrease of tone. In one instance, this was 20 mm and in another instance 10 mm, but these values seem to represent exceptions to the general tendency. The effect on movement in the duodenum was not particularly significant. In general, changes in the amplitude of movement in the duodenum are much less constant and of considerably less amplitude than in the case of the ileum.

Domenech<sup>13</sup> presented experimental and clinical evidence to show that following the induction of spinal analgesia in the dog there is a considerable, and rather immediate, augmentation of intestinal contraction, as well as an increase in the frequency of these contractions. As a result of this action, bowel contents are evacuated, and the effect persists for from one-half to one hour. This action is abolished after the injection of atropine sulphate, and paralysis of the gut ensues. A similar paralysis follows the induction of rather profound narcosis. Section of the splanchnic nerves produces an effect similar to that of spinal analgesia, which the administration of atropine also abolishes. Peritonitis, Domenech<sup>14</sup> believed, produces paralysis of intestinal movement as a result of an irritative reflex arising in the sensory terminations of the splanchnic nerves and relayed through the spinal cord. Spinal analgesia abolishes this reflex, and thereafter the intestine resumes its normal movements.

Because of the experimental evidence of Domenech<sup>14</sup> concerning the effect of spinal analgesia on the rate of peristalsis in the dog's intestines, we have carefully examined the rate of the duodenum, ileum

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13 Domenech, quoted by Rosenstein, P. and Kohler, Hans. *Med Klin* **22** 530, 1926.

14 Domenech, Olsina F. *Action de l'anesthésie rachidienne sur la motilité intestinale (étude expérimentale)*, *Presse med* **37** 66 (Jan 16) 1929.

and colon both before and after the production of splanchnic analgesia with procaine hydrochloride. This rate varies in different animals from about eleven to about fifteen contractions to the minute. Contrary to Domenech's observations, when we worked with spinal analgesia, in every case the rate following splanchnic analgesia was the same as the rate preceding the analgesia. The effect of both vagus and sympathetic action on intestinal movement would, therefore, seem to be confined to the regulation of the amplitude of intestinal movements rather than the rate of those movements. As far as the experimental observations of Domenech<sup>14</sup> are concerned, careful examination of the tracings which he presented suggests that the movements recorded by him are not purely intestinal but have transmitted respiratory pressure changes superimposed on them. We have frequently found it impossible to obtain pure intestinal motor tracings on the kymographic drum when the intestines are within the abdomen of the experimental animal, and not infrequently, even when intestinal loops containing a balloon have been removed from the abdominal cavity and have been allowed to float freely in warm saline solution, have transmitted respiratory movements been a predominating factor in the tracing. The manner of production of these respiratory excursions and transmission of the respiratory components of the tracing are not difficult to understand. Pressure is transmitted by the descending diaphragm to the stomach and also to any loops of the small bowel which may be in the immediate vicinity. If the lumen of the small intestine contains fluid, as it always does in the case of intestinal obstruction, and to a less extent if it contains gas pressure is transmitted mechanically not only from loop to loop but also directly along the entire extent of the lumen through the intermediation of the bowel contents. The respiratory component of a bowel tracing is apt to be more marked, therefore, in cases in which the lumen of the intestine is filled with fluid material than otherwise. If in the beginning a normal tracing of the intestinal movement is obtained, the rate being counted, and if, as the result of manipulation, the intestinal movement subsequently becomes complicated by a marked respiratory component, the latter tracing may easily be interpreted as a purely intestinal movement, the rate of which is the same as the respiratory rate. As the respiratory rate is normally considerably greater than the rate of the intestinal movement, one is always liable to be misled into thinking that the rate of intestinal movements has been increased, unless concomitant tracings of both respiratory and intestinal rates are obtained. Frequently even with both the respiratory and the intestinal tracings on the same drum it is difficult to say whether a pure intestinal tracing is being obtained or whether the movements of the writing point on the drum are essentially respiratory. Presumably Domenech<sup>14</sup> has been guilty in his experiments of counting an initially

pure intestinal tracing and comparing it with a subsequent respiratory one. Only in this manner do we believe that he has been able to show a change in rate as the result of spinal analgesia.

#### SPINAL ANALGESIA

In order to compare the results obtained with spinal analgesia with those obtained with splanchnic analgesia, a series of dogs was used in which both spinal and splanchnic analgesias were produced. This comparison is especially valuable because of the large number of clinical observations that have been made following the induction of spinal analgesia in cases of ileus. Wagner,<sup>15</sup> in 1922, gave the first report of the use of spinal analgesia in ileus. Since that time numerous observations have been made, especially by the French school. Asteriades,<sup>16</sup> Mauclaire,<sup>17</sup> Lapointe,<sup>18</sup> Vanlande, Boppe and Okinczyc,<sup>19</sup> Picot,<sup>20</sup> and Guibal,<sup>21</sup> Duval,<sup>22</sup> in 1927, collected 400 cases of acute ileus in which spinal analgesia had been used. Markowitz and Campbell<sup>23</sup> employed spinal analgesia in experimentally produced ileus in dogs. Their results in cases of physiologic, chemical, and traumatic ileus compare favorably with the results obtained clinically by the observers mentioned. The only investigators, besides ourselves, who have reported experiments on splanchnic analgesia are Rosenstein and Kohler,<sup>24</sup> who worked with rabbits exclusively. In attempting to evaluate their work, it should be appreciated that there is no comparison between the activity of the intestinal movement in the rabbit and that in the dog. While, when the abdomen is open, intestinal movements can be observed only once in a great while in the dog, these movements are invariably seen in the rabbit, and are often spectacular. They persist even after circulation

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15 Wagner, G. A. Zur Behandlung des Ileus mit Lumbalanesthetie, *Arch f Gynak* **192** 336, 1922.

16 Asteriades, T. Sur le traitement de l'ileus spasmodique postoperatoire aigu par la simple rachianesthetie, *Presse med* **33** 1480, 1925.

17 Mauclaire. A propos de la rachianesthetie dans l'occlusion intestinale, *Bull et mem Soc nat de chir* **53** 472, 1927.

18 Lapointe, A. La rachianesthetie dans l'ileus, *Bull et mem Soc nat de chir* **53** 479, 1927.

19 Vanlande, Boppe, and Okinczyc. Rachianesthetie et ileus, *Bull et mem Soc nat de chir* **53** 479, 1927.

20 Picot. La rachianesthetie au cours de l'occlusion intestinale, *Bull et mem Soc nat de chir* **53** 486, 1927.

21 Guibal, P. La rachianesthetie dans l'ileus, *Bull et mem Soc nat de chir* **53** 539, 1927.

22 Duval, P. La rachianesthetie dans l'ileus aigu, *Bull et mem Soc nat de chir* **53** 596, 1927.

23 Markowitz, J., and Campbell, W. R. The Relief of Experimental ileus by Spinal Anesthesia, *Am J Physiol* **81** 101, 1927.

24 Rosenstein and Kohler (footnote 1 and 10).

and respiration have ceased, and continue for some time thereafter often with great activity. Graphic representations of intestinal movements in all of Rosenstein and Kohler's investigations have been conspicuous by their absence. An unaided visual observation of moving phenomena is notoriously subject to false interpretation especially when preconceived notions exist in the mind of the observer as to what he expects to find.

While the technic of lumbar puncture is not particularly easy in the case of certain human subjects, in the case of ordinary experimental animals it is not only difficult but, in our experience, virtually impossible, at least in the dog. In this animal the dural sac may not ordinarily be punctured except at one point, caudal to the fourth lumbar vertebra. At this level there is a hiatus, through which a needle may be introduced, between the last lumbar vertebra and the ileum and sacrum. The spaces between all other vertebrae are occluded by overlapping laminae, which present a barrier to the point of the needle. Domenech<sup>25</sup> developed a technic by which he has occasionally been able to enter the dural sac by introducing the point of the needle considerably lateral to the midline and directing it medially and toward the cervical region, thereafter gradually working it between the laminae. The introduction of a needle in the ordinary manner into the only available interspace, as previously noted, is a matter of great technical difficulty, a difficulty which is scarcely appreciated when one observes the illustrations sometimes shown in books of experimental animal surgery (Haberland<sup>26</sup>), since the width of the dural sac at this point is scarcely greater than 2 mm (fig. 12) and the depth of the dural sac below the surface of the skin is 4 or 5 cm, or even more, depending on the size and the weight of the dog. In a comparatively large series of animals we have rarely been able to enter the dural sac with the point of a needle. In the case in which spinal puncture has been successfully performed, moreover, it has been found technically impossible to keep the point of the needle accurately within the dural sac so as to enable the withdrawal of cerebrospinal fluid, and a greater refinement of technic than we have been able to command would seem to be necessary to inject successfully an amount of solution sufficient to produce true spinal analgesia. This may be partly due to the additional fact that the dural sac in this particular location is surrounded by a comparatively thick and friable fat pad, obviously the introduction of a procaine hydrochloride solution must be made with considerable force in

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25 Domenech Olsina F. Estudio experimental y clinico de la accion de la anestesia raquidea sobre la motilidad intestinal. *Rev. med. de Barcelona* 7:132, 1927.

26 Haberland, H. F. O. *Die operative Technik des Tierexperimentes*. Berlin: Julius Springer, 1926.

this area, in order to insure adequate diffusion in the subarachnoid space so as to produce a spinal analgesia of sufficient height. An amount of fluid great enough to obtain this result probably always eventuates in a regurgitation of fluid through the rent in the dura into the fat pad surrounding the dural sac. Probably this cycle of events actually



Fig. 12.—The lower dorsal, lumbar and sacral portions of the spinal cord of the dog, showing an intact dura. At the lower levels the conus medullaris is visible. The marker on the left side indicates the area between the last lumbar vertebra and the sacrum, the only point at which spinal analgesia can be induced in the dog.

occurred in many of our animals, because complete relaxation of the rectal sphincters was uniformly noted, a sign which is consistently present in sacral analgesia.

We are firmly convinced that with possibly an exceedingly rare exception any attempt at the production of a high spinal analgesia in the dog results not in a spinal analgesia but in a sacral analgesia, which is easily mistaken for a true spinal analgesia by the unwary especially if a concomitant blood pressure tracing is not obtained. At least we wish to go on record to the effect that in no case has any one of the three present investigators been able even after hours of painstaking endeavor to produce an unmistakable high spinal analgesia by the introduction of a needle through the unbroken skin in the lumbar region in the dog, the success of the operation being gaged by a typical fall in blood pressure. Because of our consistent failure to obtain a true spinal analgesia in the ordinary manner, spinal puncture, we conceived the idea of performing formal laminectomy in the upper lumbar region thereby exposing the dura and subsequently injecting an anesthetic solution into the dural sac under the guidance of direct vision. Unfortunately, this method succeeds scarcely better in our hands than does ordinary lumbar puncture. Even with the dural sac thus exposed it is a matter of insurmountable difficulty to withdraw cerebrospinal fluid from the subarachnoid space, and when an attempt is made to inject an anesthetic solution, the solution can be plainly seen to exude from the dural sac through the puncture opening around the needle. We have attempted with relatively little success to avoid this regurgitation both by bending the needle and introducing it for a considerable distance along the subarachnoid space cephalad and also by attempting to compress the dura against the needle mechanically. The dura of the dog tears easily, and the introduction of a needle stimulates reflex activity to such an extent that it is a matter of considerable difficulty not only to avoid producing a rent in the dura, but even to retain the point of the needle within the dural sac. The only method by which we have been able consistently to obtain a satisfactory, true, high spinal analgesia of such a nature as to give the characteristic blood pressure decrease and splanchnic block has been formal laminectomy of the last lumbar together with the first sacral vertebra, exposure of the terminal portion of the dural sac by careful dissection of the fat pad in the vertebral canal and cannularization of the dural sac in this region under direct vision.

In connection with this discussion, it must be recalled that the stimulation of any sensory nerve trunk produces an immediate slight fall in the blood pressure. Such a fall in the blood pressure is constantly noted as the result of the mere introduction of the point of a needle through the skin, even in an anesthetized animal. Such a fall in blood pressure must not be confused with the decrease produced by a correctly given splanchnic or spinal analgesia. This pseudo-blood pressure

effect occurs immediately, is relatively slight and is usually relatively quickly compensated. On the other hand, the fall in blood pressure resulting from either splanchnic or spinal analgesia is delayed for at least a half minute, and the decrease in blood pressure is gradual and inclined to be profound, while at the same time it tends to persist for many minutes.

It should be noted in connection with the works of Domenech<sup>27</sup> that any manipulation involving the cord, inevitably produces hyperpnea. Unless one is fully aware of this fact, one may easily misinter-

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Fig. 13—Kymographic tracing, showing the effect produced on blood pressure and intestine by spinal analgesia, and the subsequent effect produced by the administration of ephedrine. In the upper tracing a distinct fall in blood pressure was produced by spinal analgesia. After about seven minutes there was an increase in intestinal movement associated with only slight increase in intestinal tone. This persisted and was evident on the lower tracing where, at 4 05 p m, 1 cc of ephedrine was injected subcutaneously. Following this there was a definite increase in blood pressure, and after about six minutes there was complete cessation of all intestinal movements, as well as a loss in intestinal tone.

pret the respiratory tracing for true intestinal movement. In this manner, changes in intestinal rate may be falsely interpreted.

One further observation in connection with diminution of blood pressure observed in spinal or splanchnic analgesia is worthy of par-

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<sup>27</sup> Domenech (footnotes 13 and 25)

ticular note. Decreases in blood pressure are frequently so profound as to cause anxiety as to the ultimate survival of the animal. Under these circumstances one naturally turns to the administration of some blood pressure raising drug especially ephedrine or epinephrine. The loss of intestinal tone following the use of these drugs is well known. Both theoretically and experimentally it is futile to expect to produce satisfactory augmentation of intestinal motility in cases in which either of these drugs has been previously administered (fig 13).

The following conclusions are based on experiments involving thirteen animals in which spinal analgesia was produced. Because of the difficulties in technique aforementioned, only seven represented cases of undoubted pure spinal analgesia. In all cases of spinal analgesia which

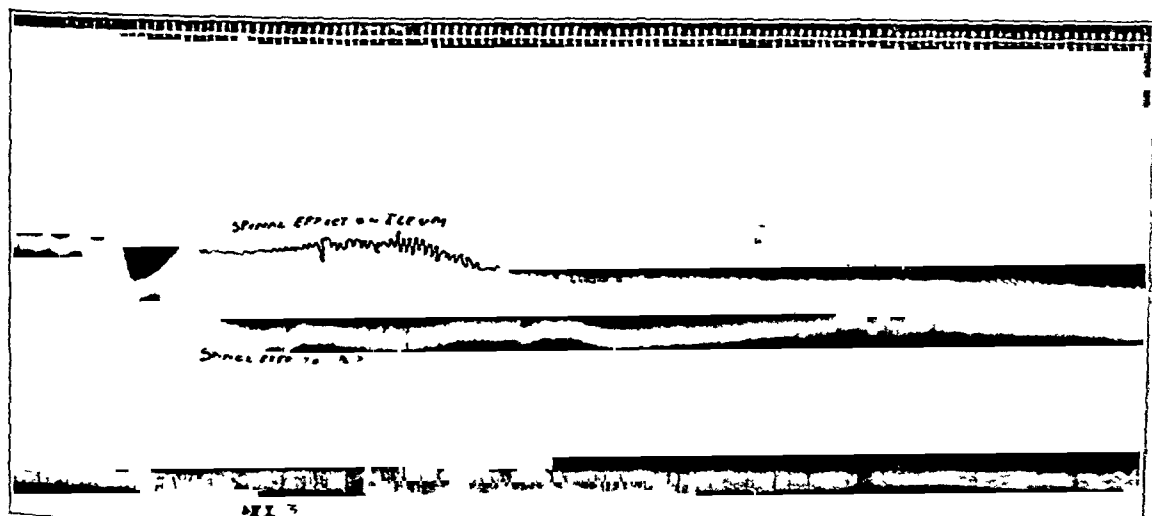


Fig 14—Kymographic tracing showing the effect on blood pressure, ileal movement and ileal tone produced by spinal analgesia. Immediately following the induction of spinal analgesia, there was a definite decrease in blood pressure which was permanent. About forty-five seconds after the fall in blood pressure became evident there was an increase in intestinal tone associated with a slight increase in intestinal movement. One minute after the intestinal tone had become maximal intestinal movement became more marked. The intestinal tone remained elevated for about three minutes, following which it fell to a normal level. The intestinal movement remained constant.

were high enough to interrupt the splanchnic fibers, definite and constant changes in the blood pressure and intestinal movements were noted. The most constantly observed phenomenon following a successfully produced spinal analgesia is a fall in blood pressure, which may occur within a half minute after the induction of spinal analgesia (fig 13). This fall in blood pressure is usually gradual, but is more rapid than that which follows the induction of splanchnic analgesia. The fall in blood pressure



resulting from a spinal analgesia is from two to three times as great as that occurring after splanchnic analgesia

Associated with, but invariably following, the decrease in blood pressure, an increase in tone, as well as an increase in intestinal movements, was noted after spinal analgesia (fig 14) The increase in tone occurring after spinal analgesia is less marked and of shorter duration than that occurring after splanchnic analgesia (fig 15) The increase in intestinal movements is, however, as constant and persists as long,

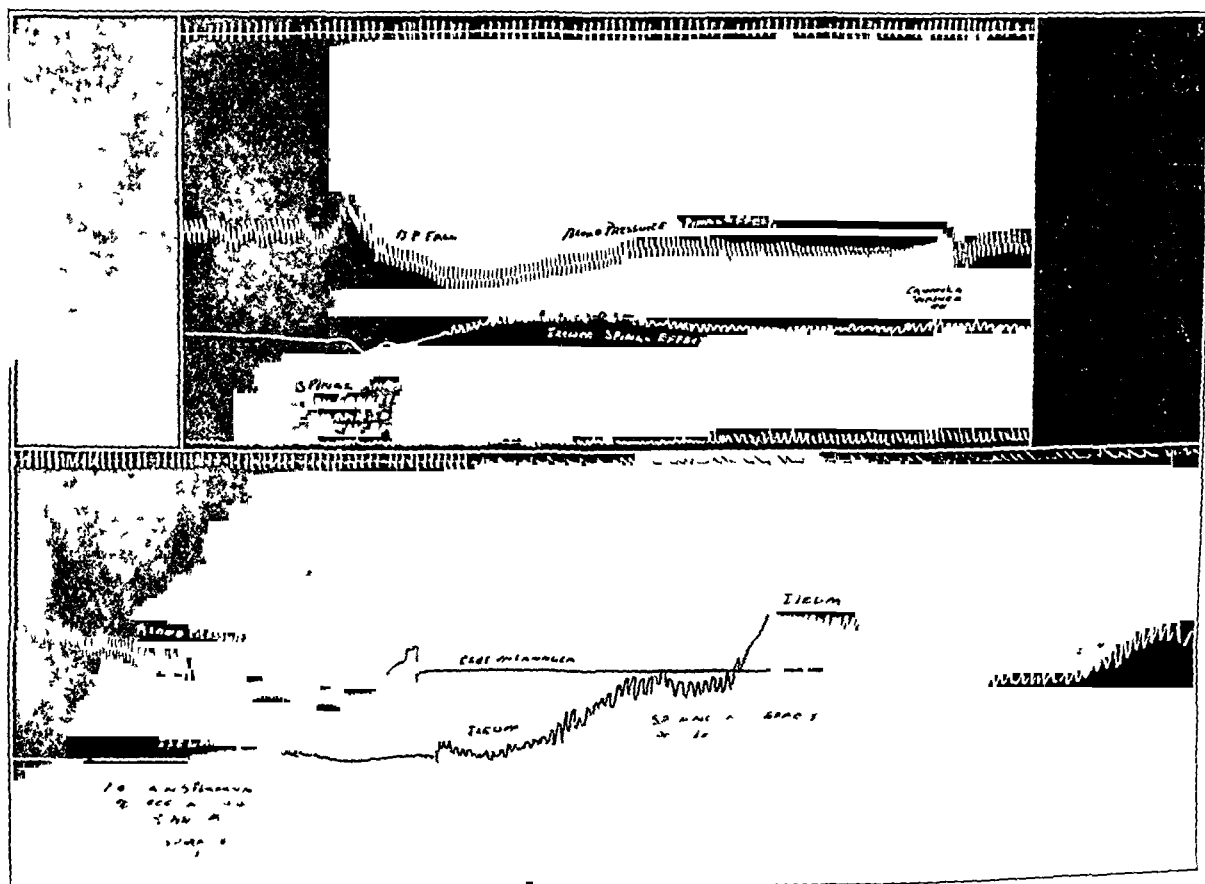


Fig 15—Kymographic tracings comparing the effect of spinal and splanchnic analgesia. The upper tracing showed the effect of spinal analgesia which was produced at the point indicated by the arrows. There was a decrease in blood pressure. After about one and one-half minutes there was a slight increase in intestinal tone followed by a definite increase in intestinal movement. The lower curve illustrates the effect produced by splanchnic analgesia, in the same animal, after twenty-eight minutes. A fall in blood pressure resulted, the carotid cannula becoming obstructed. After about three minutes there was a slight increase in intestinal movement. After five minutes the intestinal movement became much more marked and the tone increased rapidly, the increase in tone persisted for about five minutes, at which time a level was reached.

is not longer. The latent period of decrease in blood pressure following spinal analgesia is fifteen seconds and the latent period of the rise in tone of the intestine following spinal analgesia is from thirty to sixty seconds whereas the latent period of increase in intestinal activity is still longer from sixty to ninety seconds. Our tracings show that the motor effects of spinal analgesia and that the prolongation of the effect of both spinal and splanchnic analgesia are more marked in the obstructed gut than in the normal gut.

The motor response resulting from stimulation of the vagus is more pronounced and prolonged after spinal analgesia than before. This corresponds with the result one would expect to obtain if the dual motor-inhibitor-vagus-splanchnic theory is correct. In other words when chemical section of the splanchnic nerves which are inhibitory to the intestine has been produced the motor component of the extrinsic nerve supply to the intestine is alone operative. Therefore it functions without hindrance on an intestine devoid of inhibitory control. Consequently the effect of stimulation of the vagus under these circumstances is maximal. As a rule, the reaction of the blood pressure to vagus stimulation seems to be unaltered by spinal analgesia, and this is in distinct contrast to what we have previously observed in the case of splanchnic analgesia. In splanchnic analgesia the blood pressure effect following stimulation of the vagus is characteristically abolished, or at least tends to be diminished, presumably owing to diffusion of the solution used in splanchnic analgesia in such a way as to involve at least a part of the plexus cardiacus. Occasionally, as the result of splanchnic analgesia, the effect of the vagus on one side shows diminution or absence, while on the other side little effect can be noted. This lack of uniformity may be dependent either on the position of the animal during and subsequent to the administration of splanchnic block or on anatomic factors as yet undetermined. The reason why the vagus is unaffected in spinal analgesia, in contrast to splanchnic analgesia is that ordinarily the diffusion of the anesthetic solution is not high enough in the latter to affect the vagus center.

#### COMMENT

We believe that the use of nicotine in the treatment for intestinal obstruction is contraindicated not only because it is inefficient in increasing intestinal movement but because of its undesirable blood pressure raising characteristics. Amounts of nicotine sufficient to produce even noticeable splanchnic effects are capable of doubling the blood pressure. Doubling the blood pressure of certain persons clinically, especially those of advanced age and those suffering from cardiovascular disease would be a hazardous procedure. The use of this drug is definitely contra-

indicated also in view of the fact that we have a better method of blocking the splanchnic nerves, which avoids this undesirable blood pressure change, namely, splanchnic analgesia obtained with procaine hydrochloride. In several cases in this series of experiments, the animals died during the subsequent rapid fall in blood pressure following the initial rise due to nicotine. At first it was considered that the animals died as a result of nicotine poisoning, but in view of the experimental use of the much larger doses of nicotine by Rosenstein and Kohler<sup>1</sup> without fatal results, in the case of rabbits, we were forced to look further for the cause of death. We then discovered that the mechanics involved in the recording of the blood pressure tracing in our experiments were such that considerable quantities of 2 per cent solution of sodium citrate found their way almost directly into the heart of the animal during the period of rapid diminution of blood pressure. As we have been able to produce the death of animals by the rapid introduction of sufficient quantities of 2 per cent solution of sodium citrate directly into the cardiac chambers, we assume that such an occurrence explains our fatalities.

Chemical section of the splanchnic nerves, either by subarachnoid block or by an infiltration of the retroperitoneal space in the region of the splanchnic nerves, as a therapeutic measure, is open to criticism because of the fall of blood pressure which it produces. Depression of the blood pressure is more marked in spinal analgesia than in splanchnic analgesia, and for this reason spinal analgesia is probably less desirable. A decrease in blood pressure is undesirable, because patients suffering from ileus usually have a relatively low blood pressure initially. Any additional decrease in blood pressure is liable to reduce it to unsafe limits. Again we wish to emphasize the fact that the common practice of combating this fall in blood pressure with epinephrine and ephedrine, while highly desirable in spinal injection intended primarily for analgesic effect, seriously minimizes the action of spinal and splanchnic analgesia on intestinal movements (fig 14). The decrease in effect on the intestines is probably due to a sympathetic stimulation at the neuromuscular junction peripheral to the block produced by the anesthetic solution. As the splanchnic nerves are inhibitory, stimulation of them produces inhibition with resultant loss of tone and cessation of intestinal movements. This is in accord with our experimental observation in that the animals which had previously received these drugs never showed the characteristic intestinal motor effects, and in cases in which motor activity was present, the injection of these drugs speedily caused an inhibition of movements.

Considering the effect of spinal and splanchnic analgesia on motor activity, our evidence seems to show conclusively that splanchnic analgesia is preferable. The reason why splanchnic analgesia is more

efficient than spinal analgesia is by no means apparent since both procedures involve chemical section of the splanchnic nerves. The difference in effect is apparently dependent on the level at which the block is performed. We provisionally assume that the effect on intestinal tone is more marked following splanchnic analgesia than following spinal analgesia because not all the pathways of the reflex arc are involved in the inhibitory control of tone and intestinal movement pass through the anesthetized part of the cord, but that a part of the mechanism may involve the transmission of impulses through the sympathetic plexuses extradurally in which case the effect of direct infiltration of the ganglia and plexuses formed by the greater and lesser splanchnic nerves would produce a complete block, whereas subarachnoid block would produce an incomplete one.

Several investigators notably Domenich,<sup>14</sup> have assumed that intestinal paralysis in peritonitis is due to a reflex involving a sensorimotor arc through the splanchnic nerves. Domenich has shown that paralysis of the splanchnic nerves suffices to overcome the paralysis due to peritonitis. Wagner<sup>1</sup> was able to combat peritonitic ileus by the intraspinal injection of procaine hydrochloride. Apparently these authors have taken for granted that all nerve fibers entering into the formation of this arc pass through the cord. This we do not believe to be necessarily true, since the sympathetic system shows local autonomy and, while connected with the central nervous system, can function independently of it. Both clinically and experimentally the effects of spinal and splanchnic analgesia are subject to considerable variation. These variations are probably due to faults in technique. Such variations are more likely to occur in connection with splanchnic analgesia, due not only to anatomic variations in the position of the sympathetic ganglia, but also to the technical difficulty of the procedure.

In spinal analgesia, while the aspiration of cerebrospinal fluid through the needle is positive evidence that the subarachnoid space has been entered, the point of the needle may not always be maintained within the subarachnoid space during the entire period of the injection of the anesthetic agent, and moreover, the level to which the analgesia may be obtained is beyond the absolute control of the operator.

#### CONCLUSIONS

Obviously, splanchnic analgesia will be ineffective in the treatment for ileus in those cases of mechanical intestinal obstruction in which the obstruction has not been previously relieved by surgical intervention. Splanchnic analgesia is a method which should be used early and not as a last resort, since it can hardly be expected that a patient who has already absorbed a lethal dose of toxin can be revived by any means.

The accessory supportive treatment of patients with ileus should not be neglected, especially the treatment for associated alkalosis, dehydration and chloride deficiency

As experimental splanchnic analgesia produces no marked motor effect on the large intestine, we believe that in the patients treated by such analgesia the insertion of a rectal tube and the administration of an enema, in conjunction with the induction of the splanchnic analgesia, will probably be of value. In the late case, especially in the case of mechanical obstruction, at least one enterostomy should be performed prior to the induction of the splanchnic analgesia.

In those cases of peritonitis in which the peritonitic process tends to be localized, splanchnic analgesia should be used cautiously and only after due consideration, because of the danger of converting a localized into a generalized process.

While the technic of splanchnic analgesia is not particularly difficult, only one who has performed the procedure under close supervision or who has taken occasion to practice the technic on the cadaver and who is thoroughly familiar with the anatomy involved should be considered competent to perform it clinically.

Of the three general methods which have been devised for the production of splanchnic analgesia, the Wendlung technic, which involves puncture of the intact anterior abdominal wall, probably has no place in rational surgical intervention. The Braun technic involves preliminary laparotomy and somewhat extensive intra-abdominal manipulation, and is therefore practically never indicated in the treatment for ileus. The third method, the method of Kappis, which involves the introduction of a needle posteriorly through the flank, is almost invariably the method of choice in the treatment for ileus.

We recommend the use of four points of injection, as originally described by Kappis, one on either side of the midline approximately opposite the first lumbar vertebra, and one on either side below and at corresponding points opposite the second lumbar vertebra. The solution which we use and recommend is a plain 2 per cent solution of procaine hydrochloride in physiologic sodium chloride solution. Twenty cubic centimeters of the solution should be injected at each of the four points. Due to the inhibitory effect of epinephrine, ephedrine and atropine on intestinal movements, these drugs should never be used either before, with, or after splanchnic analgesia when used in the treatment for ileus.

Experimental evidence is conclusive that when nicotine is injected into the splanchnic area it is of little value in increasing intestinal movement, and is also distinctly dangerous because of its marked cardiovascular effects.

Although we have not used spinal analgesia in the treatment for ileus clinically our experimental results indicate that splanchnic analgesia is preferable to spinal analgesia in increasing intestinal movement increase in tone is especially noticeable

Blood pressure determinations should be made both before and after the introduction of an anesthetic solution into the splanchnic area, since a fall in blood pressure is invariably found after successful splanchnic blocks. This decrease in blood pressure indicates that a successful analgesia has probably resulted. While a decrease in blood pressure is theoretically undesirable, we do not believe that it ordinarily constitutes a contraindication to the use of the method as this effect is neither unduly profound nor prolonged. However it must be admitted that reduction in blood pressure is ordinarily undesirable, and this consideration should not be minimized. It constitutes one of the chief objections to spinal analgesia in which method blood pressure decreases are characteristically of greater magnitude.

Since the effect of splanchnic analgesia on the motility of the intestine is only transitory (lasting from six to thirty minutes in experimental animals), this procedure may be repeated in case the previous injection has not proved altogether successful after the lapse of as short a time as one hour.

At the risk of repetition we wish to express ourselves as of the opinion that additional stimulation of the colon by means of an enema may be of distinct value as an accessory to the induction of splanchnic analgesia because of its stimulating effects on colonic movement the colon being a part of the intestinal tract which is affected only slightly if at all, by the chemical section of the splanchnic nerves.

Our clinical observations in general surgical practice indicate that intestinal motility is much more frequently noted following splanchnic analgesia than following the induction of spinal analgesia in spite of the fact that epinephrine has been used more frequently in the former method than in the latter method.

# INFLAMMATORY CECAL TUMORS

## DIAGNOSIS OF TYPES OF OBSCURE ETIOLOGY \*

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Studies of the pathologic enlargements of the ileocecal region usually have been confined to the commoner conditions, for example, neoplasms, tuberculosis and other granulomatous processes of definite etiology. Difficulty usually does not arise in establishing the identity of a malignant condition of the cecum. Earlier diagnosis of these lesions is desirable, however. Similarly, the inflammatory swellings of definite etiology, especially tuberculosis and actinomycosis, usually are readily recognized. But there remains a conspicuous absence of early diagnostic signs.

A brief review of some of the less common cecal tumefactions seems advisable before our series of cases is presented.

Lymphomas occur fairly commonly, but in comparison to carcinomas they are rare lesions. Cinaglia<sup>1</sup> considered lymphomas in considerable detail. The closely allied condition lymphosarcoma was recently reviewed by Rankin and Chumley<sup>2</sup>.

Cholesteatoma is one of the rarest of the cecal tumors. Humiston and Piette<sup>3</sup> reported a case in 1921, and Klemptner and Palmissand<sup>4</sup> another in 1927. The latter was in a girl, aged 18, and the tumor was found in the course of operation for ruptured appendix. A glistening tumor, 7.5 by 0.5 cm., was peeled out of the wall of the cecum. They concluded that the origin of the cholesteatoma probably was an embryonic displacement of epidermal cells.

Lipoma of the cecum, like most of these lesions, has been identified only at operation. Comfort<sup>5</sup> recently reported twenty-eight cases

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1 Cinaglia, Raniero. *Linfoma dell'intestino cieco*, Policlinico **33** 1085, 1926.

2 Rankin, F W, and Chumley, C L. *Lymphosarcoma of the Colon and Rectum*, Minnesota Med **12** 247, 1929.

3 Humiston, C E, and Piette, E C. *True Cholesteatoma of the Cecum*, J A M A **84** 874 (March 21) 1925.

4 Klemptner, Dietrich, and Palmissand, D J. *Cholesteatoma of Cecum*, Illinois M J **52** 82, 1927.

5 Comfort, M W. *Submucous Lipomas of the Gastro-Intestinal Tract*, to be published.

Matry<sup>6</sup> reported a case in which intussusception resulted. The pre-operative diagnosis in these cases has usually been polyp. Although single polyps occur in the cecum, they are usually a part of a general polyposis of the colon.

Leiomyoma of the cecum has been described, and Podlaha<sup>7</sup> found a large one on the posterior wall of the cecum in a patient who was in good general condition.

Bazin<sup>8</sup> reported a congenital mucous cyst in a child 8 months of age.

Pendl<sup>9</sup> expressed the belief that hemorrhagic infarction of the cecum, with tumor formation, is caused by embolism or thrombosis of the superior mesenteric artery.

The "mobile cecum" or "pelvic cecum" associated with extreme and habitual constipation is apparently a source of trouble. Schmieden<sup>10</sup> expressed the opinion that the best treatment for this is resection. There are numerous inflammatory conditions in this region which often cause serious trouble and much diagnostic difficulty.

Although diverticulosis and diverticulitis of the right side of the colon are usually only a part of a condition of diverticulosis of the large intestine, instances of cecal diverticulitis without diverticulosis of the remainder of the colon have been noted. Cooke,<sup>11</sup> French<sup>12</sup> and Greensfelder and Hiller<sup>13</sup> called attention to the rarity of such a condition. The latter reported four cases of traumatic solitary diverticula, 2 found in the course of 5,385 major operations and 2 in 400 necropsies on adults at the Michael Reese Hospital of Chicago.

There is another and a more common pericecal and cecal inflammatory lesion, with the formation of tumor, which at times causes obstruction, and the etiology of this is even more uncertain than that of some of those noted. W. J. Mayo,<sup>14</sup> in 1888, reported cases in which typhlitis or perityphlitis gave rise to palpable tumors. Similar conditions

6 Matry, C. Lipome du caecum. Invagination. Colectomie droite. Guérison, Bull. et mem. Soc. nat. de chir. **54** 1375, 1928.

7 Podlaha, J. Leiomyoma of the Cecum, Čas. lek. česk. **63** 1585, 1924.

8 Bazin, A. I. Mucous Cyst of Caecum (Congenital), Primary Intussusception. General Considerations, Canad. M. A. J. **15** 130, 1925.

9 Pendl, Fritz. Hämorrhagischer Infarkt des Coecum, Beitr. z. klin. Chir. **145** 606, 1929.

10 Schmieden. The Mobile Cecum as a Cause of Disease, Berlin Letter, J. A. M. A. **93** 135 (July 13) 1929.

11 Cooke, A. B. When Appendicitis Is Not Appendicitis, A Case of Diverticulitis of the Cecum, J. A. M. A. **78** 578 (Feb. 25) 1922.

12 French, R. W. Diverticulitis of the Cecum with Report of Three Cases, Boston M. & S. J. **189** 307, 1923.

13 Greensfelder, L. A., and Hiller, R. I. Cecal Diverticulosis with Special Reference to Traumatic Diverticula, Surg. Gynec. Obst. **48** 786, 1929.

14 Mayo, W. J. Inflammations Involving the Cecum, Its Appendix, or Both, Tr. Minnesota State Med. Soc., 1888, p. 63.



have since been noted repeatedly Rankin<sup>15</sup> published illustrations and a description of this condition Hartwell,<sup>16</sup> in 1921 and Kolouch,<sup>17</sup> in 1923, spoke of nontuberculous inflammations of the cecum Bachlechner<sup>18</sup> stated that recurrent chronic appendicitis caused these lesions Lazarus<sup>19</sup> reported five cases of primary inflammatory tumors of the cecum without involvement of the appendix He considered trauma, infection and decubitus ulceration as factors in their etiology He made note of the fact that ileocolostomy and resection may become necessary because of inability to make a diagnosis without removing the ileocecal portion of the bowel Walters and Synhorst<sup>20</sup> called attention to the "ligneous infection" of the cecum Erdmann and Clark,<sup>21</sup> in a report of forty-eight cases in which tumors of the cecum occurred, noted that thirty-seven were caused by carcinoma, seven by tuberculosis, two by lymphosarcoma and two by chronic inflammation of undetermined etiology Nemilov<sup>22</sup> called attention to the fact that these tumors may arise after appendectomy, he expressed the belief that the silk ligature used to invert the appendiceal stump may be their point of origin He regretted the fact that neither textbooks nor surgical monographs call attention to this condition It was this relative laxness, the accompanying diagnostic difficulties and the therapeutic problems that these inflammatory tumors presented which led us to report this series of cases

The first ten cases which compose group 1 represent inflammatory lesions of the ileocecal coil which caused considerable diagnostic difficulty and which did not present a definite disease entity from the standpoint of etiology

Group 2 is made up of the next nine cases, which were particularly difficult to distinguish from the cases of group 1 Finally, they proved to be due to well recognized organic disease

15 Rankin, F W    *Surgery of the Colon*, New York, D Appleton & Company, 1926, pp 366

16 Hartwell, J A    *Non-Tubercular Inflammation of Cecum*, S Clin N Amer **1** 361, 1921

17 Kolouch, F G    *Non-Tuberculous Inflammation of Cecum*, Nebraska M J **8** 106, 1923

18 Bachlechner, Karl    *Ueber entzündliche Ileocecaltumoren*, Beitr z klin Chir **124** 103, 1921

19 Lazarus, J A    *Primary Inflammatory Tumor of the Cecum Without Appendicitis*, Am J Surg **1** 350, 1926

20 Walters, Waltman, and Synhorst, A P    *Ligneous Infection of Cecum Resulting from Subacute Appendicitis*, S Clin N Amer **6** 1203, 1926

21 Erdmann, J F, and Clark, H E    *Tumors of Cecum, Discussion and Report of Forty-Eight Cases*, Ann Surg **85** 722, 1927

22 Nemilov, Alexander    *Ueber entzündliche Dickdarmgeschwülste und ihre Bedeutung in der Pathologie des Blinddarms*, Arch i klin Chir **43** 346 1928

In the last three cases, group 3, the patients had real trouble but at times little was grossly demonstrable. If such cases are carefully chosen, they offer a field for unusual therapeutic results.

#### REPORT OF CASES

*Group 1 Inflammatory Lesions of the Ilceccal Coil Causing Palpable Tumor or Roentgenologic Deformity or Both*—CASE 1—A farmer, aged 48, came to the clinic in March, 1928, complaining of "a mass in the abdomen." Three weeks before admission he had diarrhea for one day, and two days after that he had an attack of repeated sharp pains due to gas, with much borborygmus which finally had been relieved by enemas. Following this he had been in bed for three days and had lost 10 pounds (4.5 Kg). Examination by a physician at that time revealed a slightly tender mass in the right lower quadrant of the abdomen. In a week his bowels moved regularly again, and he gained strength and felt well. At no time had any blood been seen in the stools, and he did not know that he had had fever.

General examination on admission revealed nothing of note except a mass about 8 cm in diameter, slightly tender and fixed in the right lower quadrant of the abdomen. The temperature was 98.4 F. Movements of the bowels were regular about the time he was admitted. The concentration of hemoglobin was estimated at 72 per cent, erythrocytes numbered 4,200,000 and leukocytes, 4,600 for each cubic millimeter of blood. Roentgenologic examination of the colon after a barium enema revealed deformity of the cecum in a portion corresponding to that of the palpable mass. Roentgenograms of the thorax gave negative results. There were no parasites or ova in the stools examined, and no occult blood was found. A probable diagnosis of malignant lesion of the cecum was made.

Exploration was undertaken, and ileocolostomy was done. Investigation of the lesion, with the abdomen open, suggested the surgical diagnosis of carcinoma of the cecum. Resection of the right side of the colon was undertaken later, and the pathologic report on the specimen removed was as follows: "Mucosa intact, stricture due to a chronic abscess in the walls of the ileum and cecum. No carcinoma found" (figs 1, 2 and 3).

The excellent general condition of the patient and the short history were distinctly against the diagnosis of a malignant condition. Nevertheless, the mass and deformity of the cecum placed malignancy uppermost in our minds and demanded exploration.

CASE 2—A single woman, aged 28, came to the clinic on Feb. 23, 1928, because of a lump in the lower right quadrant of the abdomen. In 1921, she had an appendectomy performed elsewhere than at the clinic. In 1922, she had begun to have burning discomfort across the upper part of the abdomen, with nausea. In 1926, a burning aching type of pain had begun with cramps about the umbilicus and in the right lower quadrant of the abdomen, these attacks had lasted for one or two days and had occurred at frequent intervals occasionally associated with vomiting, fever and bloating. In November 1926 exploration had been undertaken elsewhere, and the following report had been given: "Much straw-colored fluid found in the abdomen and a lump the size of a hen's egg in the right lower quadrant; a specimen removed failed to show tuberculosis or malignancy. After the exploration the lump had increased in size and after

roentgenologic examination the lumen of the cecum had been reported as becoming smaller. There had been no loss of weight.

On the patient's admission to the clinic, there was a movable, tender mass in the right lower quadrant of the abdomen. There was no clinical evidence of thoracic disease, but roentgenograms showed evidence of scars in both apexes, as of an old tuberculous process. On one occasion the temperature was 99.6 F. Concentration of hemoglobin was estimated at 71 per cent, erythrocytes numbered 4,600,000 and leukocytes, 6,200 in each cubic millimeter of blood. On February 24, roentgenologic examination of the colon after a barium enema disclosed a filling



Fig 1—Colon after barium enema, presenting smooth angular deformity of the cecum

defect in the cecum and ascending colon, and another roentgenologic examination, on March 14, suggested that the lesion was extrinsic to the cecum.

On March 20, exploration was undertaken, ileocolostomy was done and an indeterminate diagnosis of cecal mass was made. On April 5, resection of the right side of the colon was done, and a diagnosis was made on the basis of pathologic evidence of chronic inflammatory lesion and contraction of the lumen (figs 4 and 5).

The long history of the lesion of the right lower quadrant of the abdomen, the history of the finding of straw-colored fluid in the abdomen

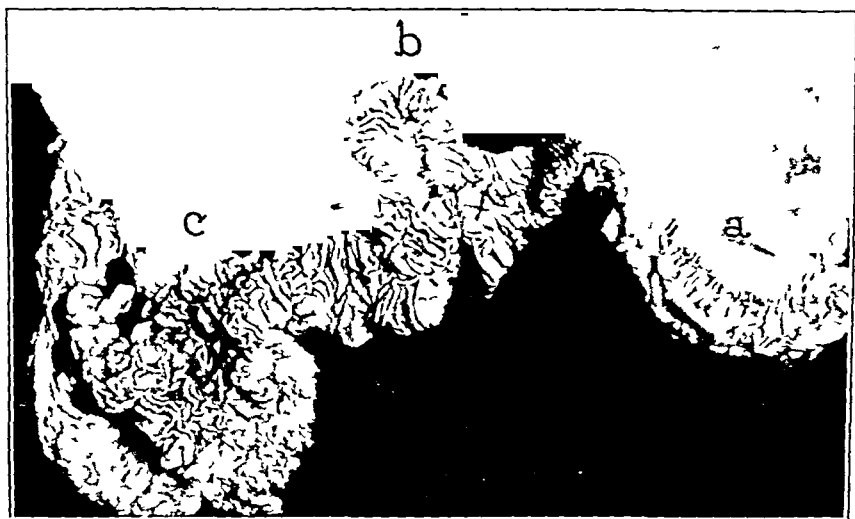


Fig 2—Cecum, ascending colon and terminal portion of the ileum opened to show the mucosa after resection, *a*, ileum, *b*, cecum, *c*, ascending colon



Fig 3—Lateral view of the cecum with section through the lesion, *a*, ileum, *b*, cecum, *c*, ascending colon

at previous exploration and the disclosure by roentgenogram of the thorax of an old, healed tuberculous lesion demanded, in spite of the negative result of the biopsy which was done elsewhere, that tuberculosis be considered. In spite of the fact that our exploration revealed only a chronic ulcerative, inflammatory lesion, it still is doubtful that we have ruled out tuberculosis in this case.

CASE 3—A man, aged 43, came to the clinic on Oct 8, 1929. He had undergone appendectomy elsewhere than at the clinic in November, 1928. For a month



Fig 4—Colon after barium enema, presenting the large defect thought to be due to a pericecal lesion

preceding this there had been recurrent attacks of abdominal distress, diffuse at first, but eventually localized more on the right side. Two weeks after the appendectomy, he had begun to have diarrhea and had averaged between five and six loose, watery stools in twenty-four hours. In June, 1929, the diarrhea had become more severe, so that he was having between twelve and eighteen loose stools, with much cramping and pain in the lower part of the abdomen. The stools had been liquid and black. Fresh blood had not been seen. There had been nausea and vomiting. In August, an abscess formed in the scar that followed appendectomy. After this abscess had formed, it had opened and closed at intervals. Six weeks before admission, the patient had lost weight and strength rapidly. His weight in health had been 170 pounds (77.1 Kg).

Examination on the patient's admission to the clinic revealed that he weighed 158 pounds (62.6 Kg). He appeared to be anemic and was markedly weak. There was generalized anasarca graded 3, in the legs and in the arms. The hemoglobin at this time was estimated at 40 per cent, erythrocytes numbered 2,010,000 for each cubic millimeter of blood. There was a firm, apparently fixed mass in the right lower quadrant of the abdomen just to the right of the old operative scar. Roentgenologic examination of the colon showed evidence of an ulcerative lesion of the ascending and transverse colon. Roentgenograms of the thorax revealed healed lesions in both apices, and there were no clinical signs



Fig 5—Resected specimen opened to show the mucosa, *a*, tip of cecum, *b*, ascending colon

of thoracic disease. The diagnosis rested between tuberculosis and chronic ulcerative colitis. The patient's condition made it inadvisable to consider surgical intervention. Measures for general upbuilding, relief from edema and transfusions were instituted, and although there was temporary improvement, the patient died on November 2. Necropsy revealed a healing ulcerative lesion of the ascending and transverse colon, a dense, fibrous stricture at the ileocecal valve and polypoid of the ascending colon (figs 6 and 7).

Any ulcerative lesion of the right side of the colon should cause tuberculosis and chronic ulcerative colitis to be included in the differen-

tial diagnosis. The roentgenologic observation of old pulmonary tuberculosis and the presence of the mass in the right lower quadrant of the abdomen indicated tuberculosis in this case. However, the absence of activity in the thorax and the absence of acid-fast bacilli in ten successive examinations of stools and sputum were decidedly against the diagnosis of tuberculosis. Necropsy disclosed chronic ulcerative colitis and polyposis. The latter is a complication that occurs in about 10 per



Fig 6—Colon after barium enema, showing the ulcerative lesion of the ascending and transverse colon and the stoppage of barium at the cecum

cent of cases of chronic ulcerative colitis. The structure of the ileocecal region has not been explained, but the effect of a foreign body must be considered in its causation.

**CASE 4**—A man, aged 36, came to the clinic on June 21, 1927, complaining of pain in the right lower quadrant of the abdomen. He said that two years before coming to the clinic his trouble had begun with cramps in the lower part of the abdomen, nausea, fever and vomiting, followed by residual soreness. In March, appendectomy without drainage had been done, followed by fever for five days, and since that time aching in this region had been continuous and had

projected toward the right hip. One month before the patient came to the clinic abdominal cramps had been worse than before and had been increased in severity by exercise, and by taking food and drink. Three weeks before he was admitted he had begun to pass watery, lumpy stools. About that time, he first noticed the mass in the right lower quadrant of the abdomen.

On the patient's admission to the clinic, except for a hard, seemingly fixed mass in the right lower quadrant of the abdomen, the results of general examination were inconsequential. The concentration of hemoglobin was estimated at 75 per cent by the Dure method; erythrocytes numbered 4,970,000 and leukocytes, 9,100 in each cubic millimeter of blood, 35 per cent of the leukocytes were lymphocytes. Roentgenologic examination of the colon after a barium enema gave a suggestion of a filling defect. The temperature was 99 F on one occasion. There was a loss of weight of 10 pounds (4.5 Kg). A diagnosis of cecal tumor



Fig 7—Specimen removed at necropsy viewed from the mucosal side, *a*, ileum, *b*, stricture, *c*, ascending colon with polyps

(carcinoma or inflammatory) was made. Exploration revealed an inflammatory tumor at McBurney's point in the abdominal wall, to which the cecum was adherent. A specimen was removed.

The shortness of the history, the sudden onset of the condition and the normal blood picture in this case were against the diagnosis of a malignant condition. The mass and the filling defect brought such a condition into consideration in the differential diagnosis.

**CASE 5**—A man, aged 53, came to the clinic on Oct 11, 1926 complaining of intermittent pain of ten years' duration in the lower part of the abdomen. The pain usually started suddenly with cramps, was worse when the patient was lying down and was relieved by voiding enemas and purging.



Except for the mass in the right lower quadrant of the abdomen, which was firm and was apparently fixed and tender, the general examination gave negative results. The concentration of hemoglobin was estimated as 76 per cent. There were 4,580,000 erythrocytes and 8,700 leukocytes in each cubic millimeter of blood. Roentgenologic examination of the colon after a barium enema disclosed a filling defect of the cecum. A diagnosis of a lesion of the cecum was made, and at exploration a diagnosis of malignant growth of the cecum. Ileocolostomy was done. Three weeks later, a second operation was done with the intention of resecting the growth. This time it was discovered that the mass had almost disappeared, it was found to be due to an appendical abscess (fig 8).

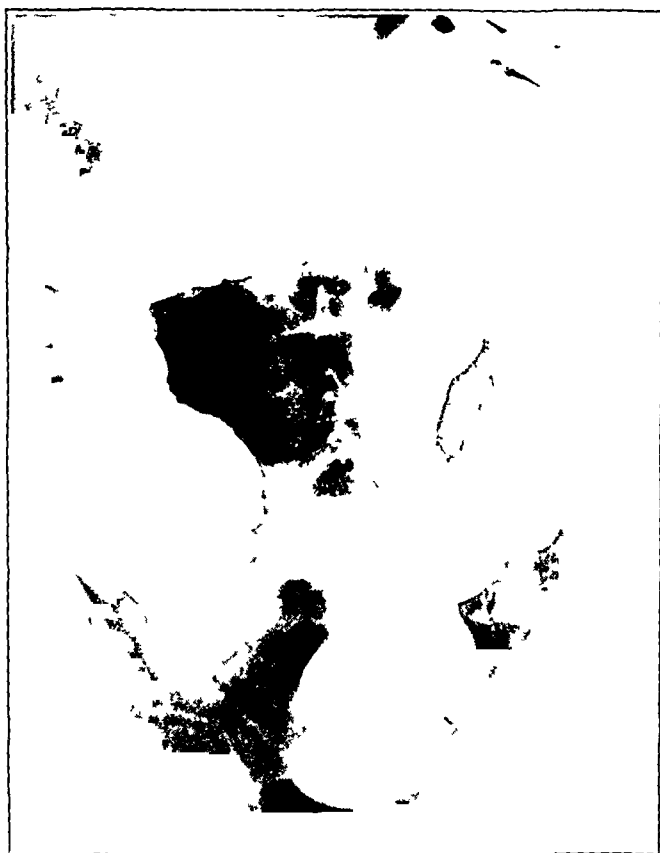


Fig 8—Colon after barium enema, presenting smooth angular deformity of the cecum (similar to that of fig 1)

The difficulty of diagnosing these lesions is illustrated in this case. Roentgenologic examination revealed a definite filling defect. The surgeon who saw the lesion thought that it was a carcinoma. A second exploration was necessary to make the diagnosis of appendical abscess.

CASE 6—A boy, aged 6 years, was brought to the clinic on March 1, 1926, with a history of intestinal trouble of five years' duration. There was a history of diarrhea beginning at the age of 10 months, of anorexia and of blood and mucus in the stools. Attacks were becoming more frequent and more severe. At no time had there been more than five or six stools in twenty-four hours.

The patient was a fairly well nourished boy, small for his age. He was 7 pounds (3.2 Kg) underweight. The temperature was 99 F on one occasion. The concentration of hemoglobin was 75 per cent, erythrocytes numbered 5,000,000 and leukocytes, 7,100 in each cubic millimeter of blood. Sigmoiditis was found on proctoscopic examination and cultures made from the lesion revealed the usual diplostreptococcus that is found in cases of chronic ulcerative colitis. Roentgenologic examination after a barium enema showed a lesion of the cecum and ascending colon and a filling defect of the cecum. A diagnosis of chronic ulcerative colitis and pericecal abscess was made.

The age of the patient, the presence of chronic ulcerative colitis and the mildness of the symptoms were against the filling defect being due to a malignant lesion. With the absence of obstructive symptoms, it seemed wise to treat the patient by medical means. A letter in October, 1929, reported that he was free from symptoms of disease of the large intestine three and a half years later.

CASE 7—A woman, aged 56, came to the clinic because of pain in the abdomen of five months' duration. The pain usually began about the umbilicus and spread to both lower quadrants and to the back, and sometimes to the left shoulder, it occurred about every ten days and lasted for several days. In the three weeks before admission to the clinic, the attacks had become frequent. There had been three severe spells, with vomiting and residual soreness. Voiding of urine was increased with the attacks.

Examination revealed a tender hard mass in the right lower quadrant of the abdomen and nothing else of note. There was a loss of weight of 4 pounds (1.8 Kg). The concentration of hemoglobin was estimated as 63 per cent, erythrocytes numbered 3,890,000 and leukocytes, 6,700 in each cubic millimeter of blood. Roentgenologic examination after a barium enema was unsatisfactory, but gave evidence of a possible lesion of the cecum. Diagnosis of tumor of the cecum was made, and at exploration a ligneous infection and subacute appendicitis were found. The appendix was removed.

The size of the tumor, the duration of the disease, the obstructive attacks from the cecal lesion and their severity would suggest inflammatory disease as the cause of the symptoms in this case.

CASE 8—A man, aged 64, came to the clinic on July 13, 1926, with a history of slight intermittent pain and soreness in the right lower quadrant of three weeks' duration. He had lost 30 pounds (13.6 Kg) in six months. He had mild diabetes.

There was a small, tender, movable mass in the right lower quadrant of the abdomen, nothing else of note was found on general examination, except marked arteriosclerosis. The concentration of hemoglobin was estimated at 73 per cent, erythrocytes numbered 5,350,000 and leukocytes, 5,600 in each cubic millimeter of blood. Roentgenologic examination following a barium enema gave evidence of slight deformity of the cecum. A diagnosis of chronic appendicitis was made. Exploration revealed subacute intestinal obstruction from adhesions about the lower part of the ileum. The adhesions were freed. It was thought that they might have caused the tumor. Because of the marked arteriosclerosis the question of a small infarct as the basis of the condition was considered.

In spite of the patient's age, the palpable tumor and the loss of weight, it would hardly seem probable that a malignant lesion would be found in this case. Exploration, with a resulting diagnosis of inflammatory disease, settled the question.

CASE 9—A woman, aged 53, came to the clinic on Feb. 10, 1926, with a history of recurrent attacks of abdominal distress, progressively increasing difficulty in moving the bowels, small stools and much borborygmus. She had had this trouble for eleven years, but had not lost weight. There seemed to be a tender mass in the region of the ascending colon.

Roentgenologic examination following a barium enema gave evidence of a lesion of the cecum and ascending colon, with a stricture at the hepatic flexure. The temperature was normal. The concentration of hemoglobin was estimated at 74 per cent. Leukocytes numbered 8,100. A diagnosis of malignant lesion of the ascending colon was made. Exploration revealed a stricture at the juncture of the cecum and ascending colon. The stricture was excised, and a plastic operation and ileocolostomy were done.

The size of the lesion and the recent increase of trouble, as well as the deformity revealed in roentgenologic examination, caused us to consider a malignant process as the etiologic factor in this case.

CASE 10—A man, aged 67, came to the clinic on Dec. 19, 1928, with a history of having had intermittent diarrhea for twenty years. He had had attacks of cramping pain in the right lower quadrant and a feeling that "stoppage" to gas and feces was taking place. The severity of the pain had increased. Analysis of gastric content done elsewhere than at the clinic showed that free hydrochloric acid was absent. Hydrochloric acid taken during the six weeks before admission had caused improvement in the attacks of diarrhea, but they had continued intermittently. He had lost 30 pounds (13.6 Kg.) in the six months prior to his coming to the clinic.

The concentration of hemoglobin was estimated at 66 per cent, erythrocytes numbered 3,350,000 and leukocytes, 6,300 in each cubic millimeter of blood. There was marked tremor of the head and body. In consultation with the neurologist, we noted early changes in the spinal cord, and the presence of combined sclerosis was considered. Analysis of gastric content after a test meal did not reveal free hydrochloric acid. Roentgenologic examination of the colon after a barium enema showed a spastic filling defect in the cecum, probably due to tuberculosis. Roentgenograms of the thorax gave negative results. A diagnosis of tumor of the cecum was made, and exploration was undertaken. A large, boggy cecum, deformed by marked adhesions between the parietal and visceral peritoneum on the right side and a chronically inflamed appendix were found. The adhesions were freed and appendectomy was done. Subsequent treatment for the anemia was instituted.

The age of the patient, the anemia and the intermittent diarrhea pointed to a lesion of the cecum. The anemia, the high color index and the early changes in the spinal cord, however, could explain the picture, except the cecal deformity, on a basis of pernicious anemia.

*Group 2. Definite Pathologic Conditions That Are Difficult to Differentiate from Those of Group 1.*—CASE 11—A man, aged 41, came to the clinic on Dec.

In 1927, complaining of stomach trouble of four years' duration. This had occurred as irregular attacks of pain and tenderness in the right lower quadrant of the abdomen. The attacks had become more severe in the year before he came to the clinic. They had occurred several hours after meals and at about 10 p. m. At times a sausage shaped tumor had appeared beneath the scar following appendectomy which had been done elsewhere in 1925. There was a history of epididymitis.

Examination revealed a tender, ballooned region in the right lower quadrant of the abdomen. The patient had lost 35 pounds (15.9 Kg) in four years. Hemoglobin was in a concentration of 65 per cent, erythrocytes numbered 4,390,000 and leukocytes, 17,500 in each cubic millimeter of blood. Roentgenologic examination of the colon after barium enema gave negative results. A diagnosis of a cecal lesion, with obstruction, was made. Exploration revealed a tumor, which appeared to be inflammatory, extending from the ileocecal juncture to the hepatic flexure. It was so large and there was so much inflammation about it, that removal was not possible. Ileocolostomy was done.

The patient returned home and made some general improvement, but five months after the first operation trouble reappeared. He returned to the clinic. Exploration at this time showed that the tumor was much larger, and the surgeon considered tuberculosis and a malignant process as possible factors in its causation. He did not attempt to remove it, because if it were tuberculous its removal would be associated with too great a risk and if malignant, it was clearly inoperable. The postoperative recovery was uneventful, and the patient returned home. It was reported several months later that he had died and that adenocarcinoma had been discovered at necropsy.

This case illustrates well the difficulty encountered in making a diagnosis of some of these cecal lesions. There was a huge tumor without evident defect in the roentgenogram, a slight degree of anemia and a fair general condition. At exploration so much secondary infection was found that a diagnosis could not be established.

CASE 12.—A man, aged 48, came to the clinic on Aug. 29, 1926, complaining of attacks of abdominal pain of nine years' duration. The attacks usually had started as "twinges" or abdominal pain, increasing to sharp "squeezing" pain which doubled him up. Pains occurred from every three to four minutes and lasted for about one minute. At the end of five or six hours of such an attack, he would vomit. Morphine sulphate had been required for relief. He had had these attacks as often as three or four times in two weeks, and sometimes had been free from them for two or three months at a time.

The temperature was not elevated. Hemoglobin was in a concentration of 74 per cent, erythrocytes numbered 4,430,000 and leukocytes, 5,000 in each cubic millimeter of blood. Roentgenologic examination of the colon after a barium enema gave evidence of a deformity of the cecum that was thought to be the result of an old inflammatory or congenital lesion. Roentgenograms of the thorax showed signs of an old bilateral pulmonary tuberculous process. Clinically, the nature of the cecal lesion was not established. Exploration revealed three hyperplastic, obstructing, tuberculous lesions, one of the cecum and two of the lower part of the ileum. These lesions caused stricture of the intestine, and ileo-ileostomy and ileocolostomy were done, which short-circuited about 90 cm. of the ileum. On account of the extent of the lesion, resection did not seem advisable. Recovery was uneventful, and the patient returned two years later in a good general condition.

This case illustrates clearly how extensive hyperplastic tuberculosis can be without producing much trouble as long as obstruction is relieved

CASE 13—A man, aged 46, came to the clinic in 1923 because of chronic ulcerative colitis<sup>23</sup> His trouble was mild, and irrigations with medicated solutions were advised He got along fairly well, he had between five and six loose stools daily, frequently mixed with blood In October, 1926, he began to have pain in the right lower quadrant, which was noted particularly before movement of the bowels About December 20, after he had carried a full sack of wheat to the top of his granary, he experienced a severe, sudden pain in the lower right part of the abdomen, followed by fever, nausea and vomiting Several days after that, he noticed a mass in the region in which he had had the pain

The patient came to the clinic again on Jan 5, 1927, at which time he was having about six rectal discharges every twenty-four hours, mixed with blood and pus, and had a rather tender mass below McBurney's point His temperature was 99 F He had lost 17 pounds (7.7 Kg) in the two months previous to admission The concentration of hemoglobin was estimated at 57 per cent, erythrocytes numbered 3,560,000 and leukocytes, 12,100 in each cubic millimeter of blood Roentgenologic examination of the colon after a barium enema showed evidence of a filling defect of the cecum and the deformity of chronic ulcerative colitis A diagnosis of chronic ulcerative colitis and cecal tumor was made Exploration revealed a tumor of the cecum that was thought to be malignant, but the tissues around it were the site of much inflammatory reaction Ileocolostomy was done on January 21 After a stormy course, the patient was discharged from the hospital and returned home He came back early in March, and his condition had improved to such an extent that on March 16 resection of the tumor, a huge lymphosarcoma, was done The patient again experienced a stormy convalescence and finally returned home About a month before this report was completed, a report showed him to be in fairly good health and back at work on his farm

Because of the presence of chronic ulcerative colitis, the sudden onset of the attack of pain and the circumstances under which it occurred, our first consideration was perforation of the cecum with abscess formation The size of the tumor, its mobility and the question of obstruction, however, made exploration advisable

CASE 14—A woman, aged 43, came to the clinic on Nov 30, 1928, complaining of cramping epigastric pain, with much rumbling The condition had been present for several years, but the attacks had increased in frequency and severity in the last few months She had lost 10 pounds (4.5 Kg) Examination revealed a mass in the right side of the abdomen which could be pushed up and down and from side to side Hemoglobin was in a concentration of 74 per cent Erythrocytes numbered 4,430,000 and leukocytes, 5,000 in each cubic millimeter of blood Roentgenologic examination of the stomach and thorax gave negative results Investigation of the colon by roentgenologic methods, after a barium enema, showed a polypoid filling defect in the distal portion of the ascending colon

Exploration revealed what was thought to be a polyp of the cecum, and ileocolostomy was performed, and later right hemicolectomy The pathologist found the lesion to be a pedunculated lipoma

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The movable mass the symptoms of obstruction and the good general condition suggested that this lesion was of the polypoid type. In the absence of lipomas elsewhere in the body it would be difficult even to suspect the nature of such a lesion.

CASE 15—A man, aged 62, came to the clinic on June 17, 1921, because of pain in the abdomen. One year prior to admission he had begun to have soreness and cramping pain in the abdomen. It had been generalized over the abdomen and had increased in severity although it had been worse in the right lower quadrant above a large inguinal hernia. There was also rather marked arteriosclerosis. Four or five months prior to admission the patient had lost 20 pounds (9 Kg).

The concentration of hemoglobin was estimated at 64 per cent, erythrocytes numbered 3,560,000 and leukocytes 5,600 in each cubic millimeter of blood. Roentgenologic examination of the colon after a barium enema gave negative results. It was thought that the large scrotal hernia or adhesions in that region might explain the distress and the patient was sent to the surgeon for herniotomy. Exploration revealed carcinoma of the cecum. Right herniotomy and resection of the ileocecal coil were performed.

The negative result of the roentgenologic examination of the colon and the presence of the large hernia misled the clinician. The attacks of obstruction, the loss of weight and the anemia would suggest a lesion of bowel. Knowledge of the fact that an occasional 'silent' carcinoma of the bowel occurs made exploration advisable here.

CASE 16—A man, aged 31, came to the clinic on May 20, 1926, because of a mass in the right lower quadrant of the abdomen which he had found accidentally two months prior to his admission. It was enlarging and occasionally he had a dull pain in the abdomen. There had been no change in the regularity of the movements in his bowels. Appendectomy had been performed elsewhere in 1916.

Examination revealed a rather firm, somewhat fixed mass in the right lower quadrant of the abdomen. There had been no loss of weight. The concentration of hemoglobin was 82 per cent, erythrocytes numbered 4,850,000 and leukocytes, 9,400 in each cubic millimeter of blood. The results of roentgenologic examination of the colon after a barium enema were reported as negative, the mass was extrinsic to the colon. The patient was sent to the surgeon with a diagnosis of a tumor in the region of the cecum. Exploration revealed an inoperable carcinoma of the posterior wall of the ascending colon with extensive metastasis in the liver.

This case illustrates the extent to which malignant lesions of the colon may advance before producing clinical signs and symptoms. In this case the roentgenogram of the colon and the blood count were negative and there was no loss of weight yet a hopelessly inoperable malignant lesion was found.

CASE 17—A woman, aged 43, a teacher, came to the clinic on June 18, 1928, with multiple complaints among them weakness. At this time there were no objective symptoms except that she weighed 4 pounds (1.8 Kg) less than she said she had weighed a year before. Prior to her coming to the clinic she had

undergone appendectomy, hemorrhoidectomy and an operation for strangulated hernia

The hemoglobin was estimated at 45 per cent the erythrocytes numbered 2,840,000 and leukocytes, 7,000 in each cubic millimeter of blood, there was some tenderness in the lower part of the abdomen

The patient was advised at the clinic to go home adopt general upbuilding measures which were prescribed and to return in two months for further observation, which she did The pain in the lower part of the abdomen had continued, although there had been improvement in the general condition She had not had diarrhea At this time roentgenologic examination of the colon disclosed a filling defect in the tip of the cecum which was thought to be due to a malignant condition Exploration revealed an inflammatory lesion of the ileocecal coil This was resected The pathologist reported a tuberculous condition There had been no evidence of tuberculosis elsewhere

This case illustrates the difficulties encountered in diagnosis of localized tuberculosis of the intestine

CASE 18—A man, aged 55, came to the clinic on June 20 1927, complaining of soreness in the right lower quadrant of the abdomen There had been a "catch" and soreness in the right lower quadrant, associated with a dull ache, for from six to eight months prior to his admission It often came on from one and a half to three hours after meals and lasted for an hour or so, it was not relieved by the taking of food or sodium There was considerable borborygmus for six months, although the regularity of the movements of the bowels had not changed He was told elsewhere that he had a tumor of the right kidney

In the right lower quadrant, examination revealed a movable mass, which seemed to be lobulated The concentration of hemoglobin was 64 per cent, erythrocytes numbered 4,360,000 and leukocytes, 11,400 in each cubic millimeter of blood Roentgenologic examination of the colon after a barium enema disclosed a filling defect of the cecum A diagnosis of a malignant lesion of the cecum was made, and exploration revealed a carcinoma of the cecum which the pathologist reported as adenocarcinoma

The only striking feature in this case was the size and mobility of the tumor without any particular symptoms referable to the bowels

CASE 19—A man, aged 44, a carpenter, came to the clinic on Dec 12, 1927, with a story of having had three attacks of pain in the right lower portion of the abdomen, with vomiting in the last two years The last attack had occurred in January, at which time there had been pain, vomiting and fever An operation had been done elsewhere, at which time an appendical abscess had been drained The appendix had not been removed, and a fistula had persisted since the operation It had been difficult to move the bowels since the time of the operation

Examination revealed a somewhat undernourished man, who weighed 20 pounds (9 Kg) less than he said he had been accustomed to weigh There was a draining sinus in the right lower part of the abdomen, about which there was considerable induration Examination of the material which drained from the fistula did not reveal sulphur bodies or acid-fast bacilli The concentration of hemoglobin was estimated at 73 per cent, erythrocytes numbered 4,760,000 and leukocytes, 8,200 in each cubic millimeter of blood A diagnosis of appendical abscess was made, and exploration revealed colloid carcinoma and a fistula The pathologist's report was colloid carcinoma with lymphatic involvement

The history of attacks of pain and of drainage of what seemed to be an appendiceal abscess together with the absence of specific inflammatory disease suggested the diagnosis of appendiceal abscess with fistula. The increasing difficulty in moving the bowels and the persistent sinus would suggest the advisability of further investigation of the large intestine.

*Group 3. Marled Obstipation in Which So-Called Pelvic Cecum Caused Difficulty in the Differential Diagnosis*—CASE 20—A man, aged 48, came to the clinic on Dec. 16, 1927, complaining of "stomach and bowel trouble" of many years' duration. Constipation had been lifelong. Appendectomy had been done in 1912 without effect on the constipation. For twenty-five years spells had occurred every two or three months and had lasted from one to two hours in which pain in the epigastrium had come on before breakfast and again at 10 a. m. and at 3 and 8 p. m. These spells had been associated with physical and mental fatigue and depression. After a spell there had been severe muscular pains, especially lumbago, so severe that he had had to go to bed. These spells had been associated with bloating, obstipation, pressure pain in the epigastrium and some tenderness and fever.

Results of examination for organic disease were essentially negative. The concentration of hemoglobin was estimated at 73 per cent, erythrocytes numbered 4,540,000 and leukocytes 7,600 in each cubic millimeter of blood. A note was made by the clinician of constipation, graded 4. Roentgenograms of the colon after a barium enema were negative, but an examination made to determine the presence or absence of gastro-intestinal stasis revealed a moderate amount of barium in the cecum and transverse colon forty hours after its administration. A diagnosis of intestinal stasis, with partial obstruction, was made. Exploration revealed a large, prolapsed cecum, and ileocolostomy and subsequently right hemicolectomy were performed. The patient has enjoyed normal health since the operation.

CASE 21—A married woman, aged 40, came to the clinic on Nov. 10, 1927, complaining of enlarging abdomen and pain in the back. She had undergone appendectomy in 1915, and perineorrhaphy in 1926. She had so-called influenza in February, 1927. About July and August, the cramping of muscles and slowly progressive increase in the size of the abdomen were noted. Movements of the bowels had been regular until about a month before admission. Since then, there had been a few spells of mild diarrhea.

Examination revealed a movable mass in the right lower quadrant of the abdomen. The tumor did not seem to be palpable on pelvic examination, and on the following day it could not be palpated in examination of the abdomen. The blood count was within normal limits. Roentgenographic examination of the colon and thorax gave negative results. The possibility of a mesenteric cyst or of a pedunculated ovarian cyst was raised, and exploration was advised. This revealed a redundant, prolapsed cecum lying low in the pelvis, and a modified Waugh operation was done.

CASE 22—A woman, aged 63, came to the clinic on July 1, 1926, complaining of increasing constipation, much gas, bloating and loss of weight.

Examination did not reveal gross abnormalities. The patient weighed 15 pounds (6.8 Kg.) less than she said she customarily weighed. The concentration of hemoglobin was estimated as 72 per cent, erythrocytes numbered 4,370,000 and leukocytes, 9,800. Roentgenologic examination of the colon after a barium enema



disclosed a filling defect of the cecum. Roentgenograms of the thorax gave negative results. In the absence of other suggestive signs and symptoms, the diagnosis could be carried no further than suspected lesion of the cecum. Exploration revealed adhesions between the cecum and lateral abdominal wall, but no tumor to cause the filling defect. There was also chronic cholecystitis with chronic cholelithiasis and a chronically inflamed appendix.

Cases 20, 21 and 22 belong in a group in which diagnosis and treatment are particularly difficult. An extensive resection such as that employed in case 20 would be unsuitable in many such cases because of surgical risk, and because it is most difficult to pick out just the right cases in which this procedure is helpful. In case 20 the patient has remained entirely free from symptoms for more than a year. Prolapse of the cecum into the pelvis has been frequently described. The fact that it sometimes causes a palpable tumefaction and even deformity, revealed by roentgenologic examination, indicates exploration as the best means of learning the method by which relief can be given. Furthermore, other conditions are found often enough to aggravate or account for the symptoms. Although undoubtedly there will be cases in which surgical measures will not be helpful, it seems best that operation be undertaken in most of them.

#### COMMENT

In any differential diagnosis of tumors of the ileocecal region, malignant disease must be given first consideration. Carcinoma is the most common of the malignant conditions, lymphosarcoma occurs rather rarely. Hyperplastic tuberculosis also has some significance. Actinomycosis is rare. The other benign tumors, such as cholesteatoma, lipoma, leiomyoma, mucous cyst and hemorrhagic infarction are rare and yet must be considered in the differential diagnosis.

It is gratifying to establish without exploration that the lesion is not malignant, but to be certain of this is difficult. Renal enlargement and retroperitoneal lesion should not be difficult to distinguish from ileocecal lesion. The roentgenogram has in a large measure done away with the former differential difficulty. The greater difficulty in diagnosis is that illustrated in the first ten cases of this series. In such cases there are a palpable mass and positive roentgenologic data, and yet the appearance of the patient is not that of the usual one presenting a malignant lesion in this situation. In these cases, the history offers the most important clue. The usual absence of anemia and the patient's general sense of well-being also offer important differential suggestions. Finally, the roentgenogram should be carefully studied to determine whether or not there is a filling defect typical of a malignant condition, this type of filling defect is rarely present in such cases.

# OCCUPATIONAL THERAPY IN THE TREATMENT OF FRACTURE OF THE JOINT\*

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1921

Three and one half years ago Dr. Carl G. Burdick, director of the fourth surgical division, Bellevue Hospital, formulated certain principles for the care of patients with acute fracture. At that time it was decided to use occupational therapy in preference to massage and physiotherapy in the treatment of fracture of the joint. On the children's surgical service Dr. Burdick had encountered six cases of myositis ossificans in fractures about the elbow. In all of these cases massage had been used and this was considered the etiologic factor in producing the myositis. Therefore it was thought that vigorous massage might produce the same changes in adults, though to a lesser degree.

## MYOSITIS OSSIFICANS

The following cases of myositis ossificans occurred in the children's surgical service.

CASE 1—A child, aged 10, received a fracture of the internal condyle of the humerus on Aug. 9, 1920, and was referred for baking and massage to overcome the restriction in the motion of the elbow. Figure 1A shows the bony changes in the muscle around the elbow. This picture was taken four months after the injury. After baking and massage were discontinued the condition improved. Figure 1B shows most of the callus absorbed; the roentgenogram was taken seventeen months following the injury, or thirteen months following figure 1A.

CASE 2—A patient, aged 10, received a fracture of the internal condyle of the humerus on July 23, 1920, and was given baking and massage. The original plates which showed the bony changes in the muscles, could not be found, but figure 2, which was taken one and one-half years following the accident, showed bony changes in the muscle.

The other cases in this series showed similar conditions and for that reason are not presented.

## USE OF OCCUPATIONAL THERAPY IN FRACTURE

During the past three and one-half years 843 fractures have occurred in the fourth surgical division, of this number, 612 have been referred to the occupational therapy department. For the past six months, 68 cases have been referred for occupational therapy, including 19 cases

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\* Read before the American Occupational Therapy Association, Atlantic City, N. J., June 18, 1929.



Fig 1—*A*, roentgenogram taken four months after injury showing bony changes in muscle around elbow following baking and massage, *B*, roentgenogram taken seventeen months following injury showing most of the callus absorbed

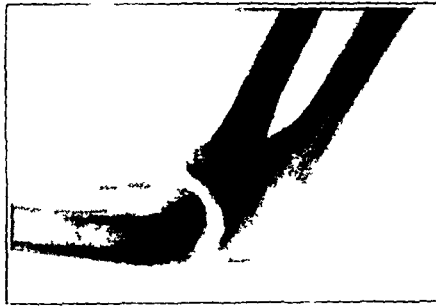


Fig 2—Roentgenogram taken one and one-half years following accident still showing some bony changes in muscle around elbow

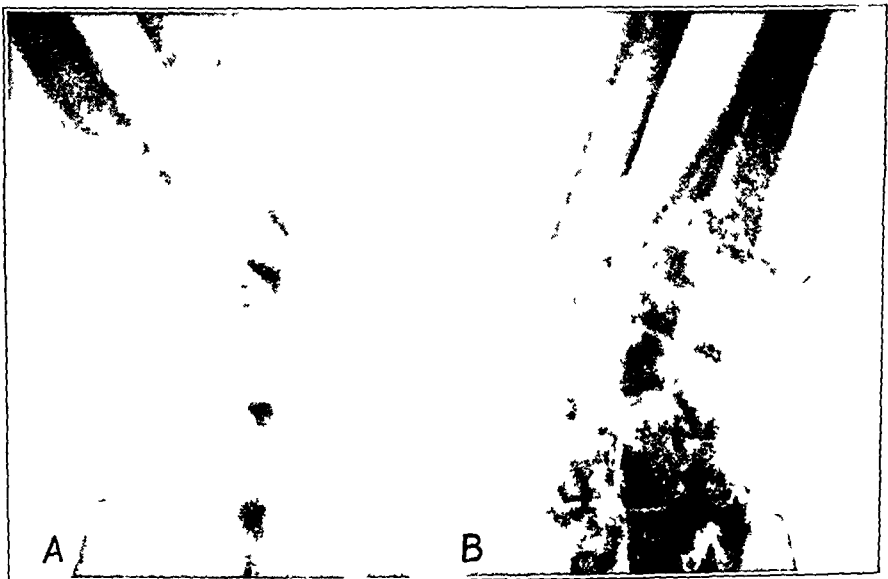


Fig 3—*A* comminuted fracture of the lower end of the radius before reduction, *B*, same fracture after reduction

of the hand 1 of the wrist 2 of the forearm 3 of the elbow 4 of the upper arm 5 of the shoulder 6 of the neck 7 of the head 8 of the face 9 of the mouth 10 of the tongue 11 of the throat 12 of the larynx 13 of the trachea 14 of the bronchi 15 of the lungs 16 of the pleura 17 of the diaphragm 18 of the pericardium 19 of the heart 20 of the aorta 21 of the pulmonary artery 22 of the pulmonary vein 23 of the coronary artery 24 of the coronary vein 25 of the inferior vena cava 26 of the superior vena cava 27 of the right atrium 28 of the right ventricle 29 of the left atrium 30 of the left ventricle 31 of the interventricular septum 32 of the interatrial septum 33 of the mitral valve 34 of the aortic valve 35 of the pulmonary valve 36 of the tricuspid valve 37 of the bicuspid valve 38 of the aortic arch 39 of the descending aorta 40 of the ascending aorta 41 of the thoracic aorta 42 of the abdominal aorta 43 of the common iliac artery 44 of the external iliac artery 45 of the internal iliac artery 46 of the common femoral artery 47 of the superficial femoral artery 48 of the deep femoral artery 49 of the popliteal artery 50 of the anterior tibial artery 51 of the posterior tibial artery 52 of the peroneal artery 53 of the fibular artery 54 of the tibial artery 55 of the plantar artery 56 of the digital artery 57 of the pharynx 58 of the esophagus 59 of the stomach 60 of the duodenum 61 of the jejunum 62 of the ileum 63 of the cecum 64 of the sigmoid colon 65 of the rectum 66 of the anal canal 67 of the prostate gland 68 of the ureter 69 of the bladder 70 of the urethra 71 of the penis 72 of the vagina 73 of the uterus 74 of the fallopian tube 75 of the ovary 76 of the endometrium 77 of the myometrium 78 of the perimetrium 79 of the cervix 80 of the hymen 81 of the clitoris 82 of the labia majora 83 of the labia minora 84 of the clitoral hood 85 of the clitoral prepuce 86 of the clitoral frenulum 87 of the clitoral ligament 88 of the clitoral suspensory ligament 89 of the clitoral bulb 90 of the clitoral gland 91 of the clitoral duct 92 of the clitoral opening 93 of the clitoral canal 94 of the clitoral sheath 95 of the clitoral skin 96 of the clitoral mucosa 97 of the clitoral epithelium 98 of the clitoral connective tissue 99 of the clitoral blood vessels 100 of the clitoral nerves



Fig 4—A, a patient doing block printing to increase flexion and extension of the wrist, B, the patient using a hammer to increase the grasping power of the hand

Miss Mary E. Merritt, director of the occupational therapy department at Bellevue Hospital, is responsible for the outline of treatment for the individual cases, and for the general supervision of the work. Casts are removed and occupational therapy is started early in all types of cases as a general rule, in ten days for Colles' fracture or for fractures about the wrist and in two or three weeks for Pott's fracture or for fractures about the ankle. The treatment for other types of fractures depends on the individual case. These patients report for treatment three times a week during each visit they receive three work periods, alternating with rest periods. The work periods vary from three to ten minutes or until the patients become fatigued. They are



Fig 5—*A*, exercise done at home to increase the motion of the fingers, *B*, exercise done at home to flex and extend the wrist

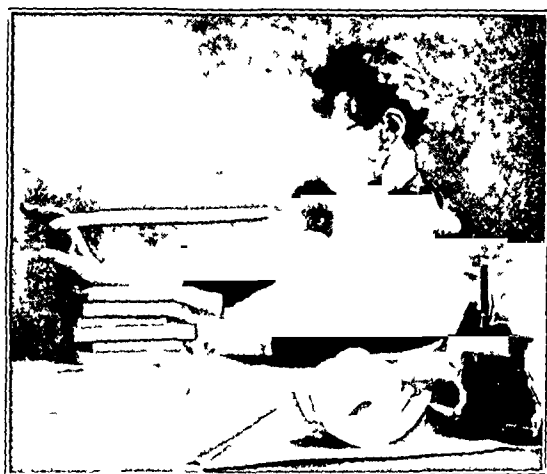


Fig 6—A patient who could not be interested in block printing is obtaining flexion and extension with an elastic band



A

B

Fig 7—A, extension and pronation of the forearm B, flexion and supination of the forearm

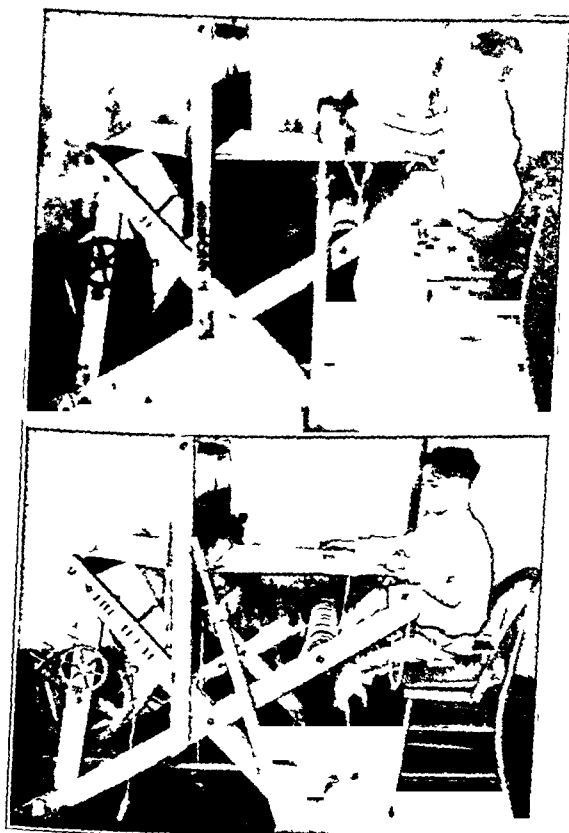


Fig 8—A, extension and pronation of the forearm B, flexion and supination of the forearm

then given a rest period of five minutes, followed by a second work period. This again is followed by a rest period of five minutes, and finally a third work period. The work periods are gradually increased and the rest periods diminished as the patients progress during the course of treatment.

*Fractures About the Wrist*—Fractures about the wrist constitute the highest percentage of the cases seen. Figure 3*A* shows a comminuted fracture of the lower end of the radius before reduction, figure 3*B* was taken after reduction. This represents a difficult case. To get a good functional result in this type of fracture, motion should be started within fourteen days. When first referred for treatment, the patient is given block printing to do, as illustrated in figure 4*A*.



Fig 9—Flexion and extension of the forearm

and *B*. This improves the grasping power of the hand, and increases flexion and extension of the wrist. A tack hammer is used at the beginning and the weight of the hammer is increased until the patient can use a 10 ounce hammer. In addition, the patients are given exercises to do at home as illustrated in figure 5*A* and *B*. In figure 5*A* the patient holds the fingers and thumb extended and touches each finger to the thumb ten times, night and morning. This number is increased until the exercise is done twenty times. Figure 5*B* shows the hands clasped together, the wrist is flexed and extended ten times, night and morning, and this is gradually increased to twenty times. Some patients cannot be interested in block printing. Figure 6 demonstrates a patient using an elastic band to obtain flexion and extension of the wrist.

*Fractures About the Elbow*—In these cases early motion is essential, and damage can be done by vigorous massage, as was illustrated in

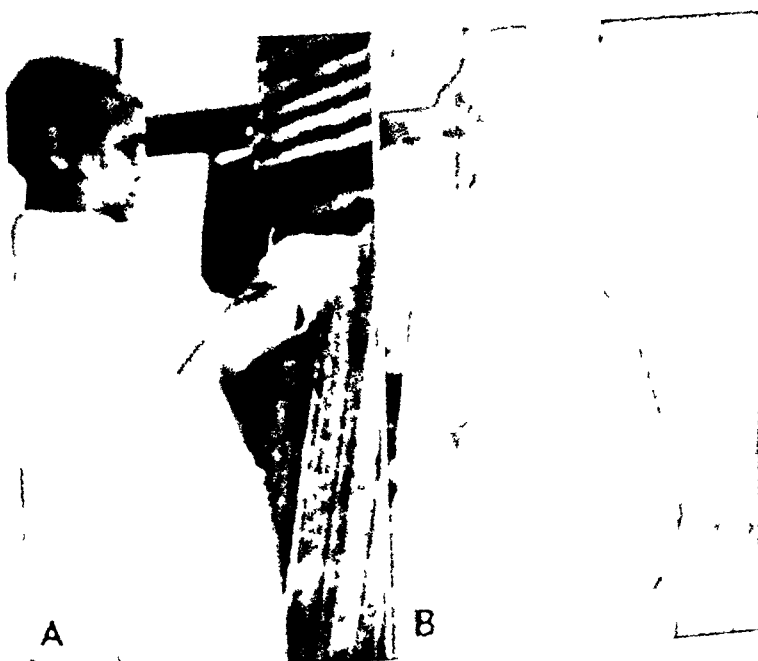


Fig. 10— different method of obtaining flexion of the forearm *B* extension of the forearm



Fig 11—Exercise done at home in cases of fracture of the elbow

patient obtaining extension of the elbow and pronation of the forearm in figure 8*B* he is obtaining flexion of the elbow and supination of the forearm, while in figure 9 the patient is obtaining flexion and extension. For patients who cannot be interested in this type of work figure 10.4 illustrates how flexion of forearm is achieved by a different method





Fig 12—Fracture of the surgical neck of the humerus

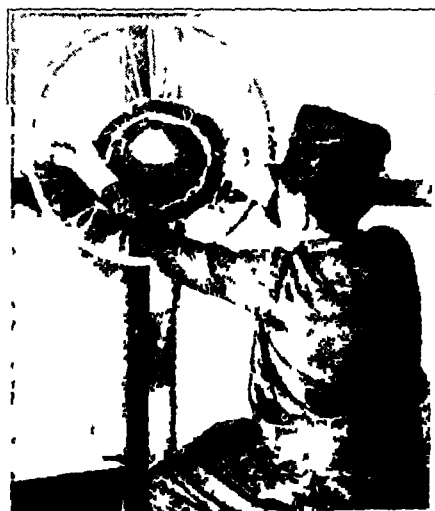


Fig 13—Abduction and extension of the arm above the head during treatment

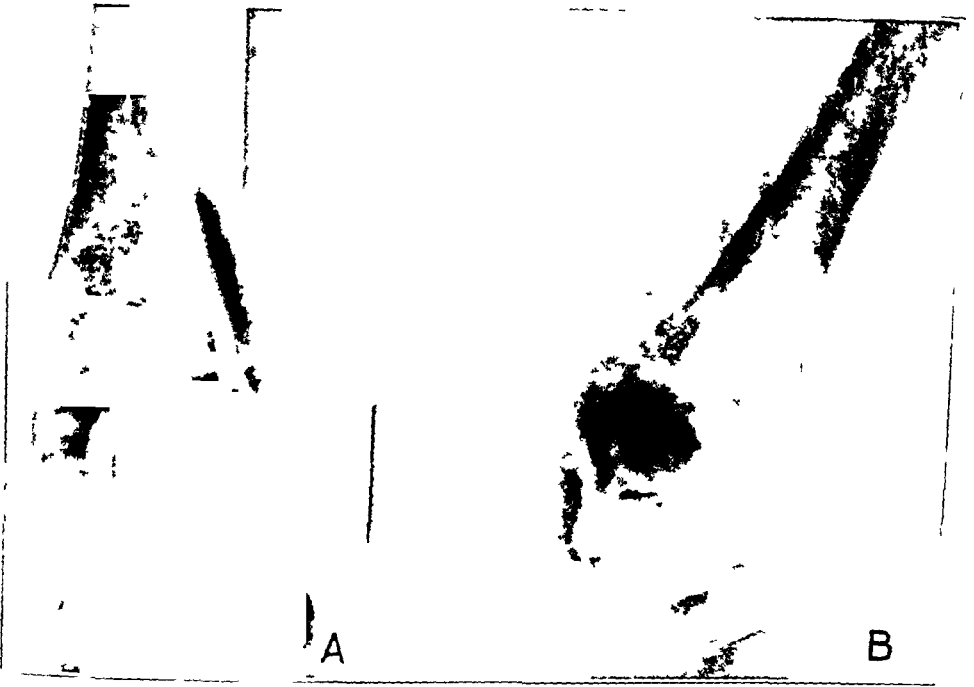


Fig 14—*A*, anteroposterior view of a fracture of the lower end of the humerus  
*B*, lateral view of the same fracture



Fig 15—*A*, anteroposterior view of the fracture shown in figure 14 after reduction, *B*, lateral view after reduction

Figure 10B illustrates extension of the forearm, while figure 11 illustrates the exercise which is done ten times night and morning at home in cases of fracture of the elbow, it is gradually increased to twenty times

*Fractures About the Shoulder*—This type of fracture is frequently seen in elderly people. Figure 12 shows a fracture of the surgical neck of the humerus. It is important to obtain abduction of the arm from the body and extension above the head. Figure 13 shows the patient accomplishing both during treatment.



Figure 16



Figure 17

Fig 16—A patient using the treadle saw to improve the motion of the ankle.

Fig 17—Articles completed by a patient during a six weeks' period of treatment.

*Fractures About the Ankle*—Next to injuries of the wrist fractures about the ankle are seen most frequently. Figure 14A is an anteroposterior view of a fracture of the lower end of the tibia and fibula. Figure 14B is a lateral view of the same fracture, while figure 15A is an anteroposterior view after reduction, and figure 15B a lateral view after reduction. It is important to obtain early motion in this type of case. Figure 16 demonstrates a patient sawing wood on a treadle saw, the foot piece of which is similar to that of a sewing machine. First, the patient is given soft white wood one fourth of an inch thick, he makes a small object, such as a shade pull. The thickness of the wood



Fig 18—*A* fracture of the patella, *B* the same fracture after operation



Fig 19—Fracture of the external tuberosity of the tibia extending into the joint

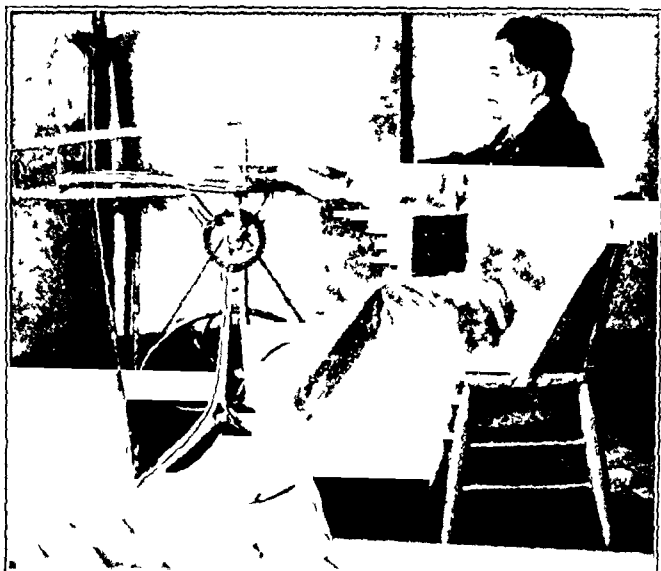


Fig 20—A patient using a machine for flexion and extension of the knee



Fig 21—A patient who could not be interested in machine work using an elastic band

is gradually increased as the patient's condition improves the size of the object sawed is also increased. During the rest period the patient sandpapers the wood puts the article together and finally paints it. Figure 17 represents the articles made by a patient with a fracture about the ankle during a six weeks period of treatment. These articles were entirely completed by the patient. The ones at the top of the picture are small and are made of thin wood while those at the bottom are larger and of heavier wood.



Fig 22—Central fracture of the acetabulum

*Fractures About the Knee*—It is important for patients with this injury to be able to obtain 90 degrees of flexion. Figure 18A shows a fracture of the patella. Figure 18B shows the same fracture after an open operation had been performed, and the ligamentum patellae and capsule had been sutured with fascia lata. Figure 19 shows a fracture involving the external tuberosity of the tibia and extending into the knee joint. Figure 20 shows the patient working on a machine with a yardstick attached for the purpose of measuring the increase in flexion and extension. Figure 21 shows a patient who could not be interested in any machine work and who obtained flexion by means of an elastic.



Fig 23—The fracture shown in figure 22, after a Steinman pin had been inserted through the greater trochanter, the roentgenogram was taken twelve hours after the insertion of the pin



Fig 24—*A* flexion of the knee and hip, *B*, extension of the leg

*Fractures About the Hip*—Fractures about the hip are represented by fractures of the neck of the femur and by fractures involving the acetabulum of the pelvis. Figure 22 shows a central fracture of the acetabulum. Figure 23 shows the same fracture after reduction has been accomplished by means of a Steinman pin inserted through the greater trochanter. Figure 24A shows the patient obtaining flexion of the knee and hip while figure 24B shows extension of the leg. Figure 25 illustrates the method of obtaining abduction of the thigh. In all types of fracture exercise was prescribed for night and morning at home.



Fig. 25—Abduction of the leg

Miss Meritt had occasion to observe patients with fractures, referred from other surgical divisions in the hospital, on whom occupational therapy and massage were employed, but these patients did not progress so satisfactorily as those on whom occupational therapy alone was used. It is essential to have trained instructors to supervise the work. One instructor can treat twenty patients in half a day.

All patients with fractures of the joint in the fourth surgical division are referred for treatment to the occupational therapy department, in preference to the department for physiotherapy.



# CORRELATIONS OF INTERNAL AND EXTERNAL PANCREATIC SECRETION

## IV EFFECT OF ISOLATION OF TAIL OF PANCREAS ON CARBOHYDRATE METABOLISM \*

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DOROTHY HENDERSON, B.A.

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CHICAGO

In previous communications, one of us (G. de T<sup>1</sup>) reported studies of the histology of the tail of the pancreas after it had been excluded from the rest of the gland and its external secretion had stopped. The splenic portion of the pancreas was isolated in twenty-five dogs, and specimens were taken from two days to one year at intervals. After a short period of edema, a gradual increase in connective tissue occurred, first around and then within the lobules, resulting in a pancreatic cirrhosis. The ducts were first dilated, then showed proliferation and infolding of their epithelium. A number of minute ducts appeared. The islands showed edema for the first two weeks, later large solid cell complexes appeared showing the vascular arrangement and staining properties of islet tissue. Such an isolated tail did not tend to degenerate and undergo absorption for at least three months if a free transplant was made into the omentum.

Furthermore, one of us and Nathanson,<sup>2</sup> in studying the diastase content in the blood following ligation of the tail, found that the high diastase values returned to normal in two weeks. In later experiments, it was found that even after artificial stimulation the diastase would not rise above the normal limits after three weeks.<sup>3</sup>

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\* From the Departments of Surgery and Physiology, Northwestern University Medical School, with the aid of an Elizabeth J. Ward Fellowship in Surgery.

1 De Takats, G. Correlations of Internal and External Pancreatic Secretion I. General Considerations and Review of the Literature, Arch Surg **19** 771 (Nov.) 1929. II. The Histologic Changes in the Isolated Tail of the Pancreas, *ibid* **19** 775 (Nov.) 1929.

2 De Takats, G., and Nathanson, I. T. Correlations of Internal and External Pancreatic Secretion. III. The Effect of Ligation of the Tail of the Pancreas on Diastase in the Blood, Arch Surg **19** 788 (Nov.) 1929.

3 De Takats, G., and Nathanson, I. T. Unpublished data.

Thus we have evidence of a persistence and even a hyperplasia of the islet tissue with histologic and chemical evidence that the external secretion has subsided from the isolated tail of the pancreas. The tail of the gland wrapped up in omentum to ensure better vascularization and possibly counteract a progressing sclerosis has been turned into a ductless gland.

The purpose in this paper was to try to demonstrate the function of this separated tail. The hypertrophy and numerical increase of islets if they are functioning might manifest themselves in an increased insulin output from the gland. Selection of a suitable method for demonstrating an increase in insulin seemed desirable.

#### SELECTION OF METHOD

Direct evidence of an increased output of insulin would be the determination of insulin in the blood and tissues of experimental animals before and after such operations. However, this laboratory has not been successful up to the present time in determining insulin in the blood of normal animal or man either with the Doisy-Somogyi and Shafer or with the Dickens and Dodds or the Moloney-Findlay method.<sup>4</sup> Another possibility, namely, the demonstration of increased dextrose-fixation of the red cell, as suggested by Loewi and Hausler,<sup>5</sup> was considered but abandoned as the reaction did not seem specific and could not be reliably reproduced later by the originator of the method.<sup>6</sup>

We had to content ourselves then with a search for indirect evidence, namely, through the action of insulin on carbohydrate metabolism. Mansfeld,<sup>7</sup> who was first to suggest an increase in sugar tolerance following ligation of the tail, used an oral sugar tolerance test to demonstrate a better utilization of carbohydrates. He emphasized the appearance of a starvation hypoglycemia after forty-eight hours of fasting, which was not present in the normal animal. He also reported a lowering of the blood sugar during fasting following ligation of the tail.

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4 Ivy, A. C. Personal communication to the authors.

5 Loewi, O., and Hausler, H. Ueber hormonale Vorgänge nach Glukose-zufuhr, *Arch f exper Path u Pharmakol* **123** 88, 1927.

6 Loewi, O. Insulin und Glykemin, *Klin Wchnschr* **8** 391 (Feb 26) 1929.

7 Mansfeld, G. Versuche zu einer chirurgischen Behandlung des Diabetes, *Klin Wchnschr* **3** 2378, 1924, Versuche zu einer operativen Behandlung des Diabetes, *ibid* **6** 105, 1927. Mansfeld, G., and Szirtes, L. Ueber die Beziehungen zwischen ausserer und innerer Secretion der Drüsen, *Arch f exper Path u Pharmakol* **130** 1, 1928. Mansfeld, G., and Schmidt, F. Versuche zu einer chirurgischen Behandlung des Diabetes, *Klin Wchnschr* **7** 1457 (July 29) 1928.

Alpern and Leites,<sup>8</sup> Nather, Priesel and Wagner,<sup>9</sup> Jorns<sup>10</sup> and Alpern and Besuglow<sup>11</sup> confirmed the observation of increased sugar tolerance following ligation of the tail. Nather, Priesel and Wagner in their second article,<sup>12</sup> Wohlgemuth and Seo,<sup>13</sup> Galehr and Ladurner and Unterrichter<sup>14</sup> could not confirm Mansfeld's results.

Jorns<sup>15</sup> in a most comprehensive work on this subject, analyzed the differences in the animals used for experimentation and the discrepancies of surgical technic that may have influenced the results.

Alpern and Besuglow<sup>11</sup> noted changes in fat tolerance after the ligation of the tail, and noted an increase in the weight of the dogs operated on. Furthermore, a change in the potassium-calcium ratio and an increase in alkali reserve were noted. This would indicate a diminution in sympathetic tonus exactly the opposite of what Wohlgemuth<sup>13</sup> found.

Realizing that none of these methods would offer a direct proof of increased insulin output, and that none of them would consider the compensatory attempts of the normal animal, even if such increased secretion were present, we selected methods that would give at least indirect evidence that a change in carbohydrate utilization had taken place.

#### FACTORS THAT INFLUENCE SUGAR TOLERANCE

A sugar tolerance curve is the result of several factors, which must be considered briefly.

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8 Alpern, D., and Leites, S. Ueber den Einfluss der Unterbindung des Ductus pancreaticus auf den Blutzucker, *Klin Wchnschr* **4** 1551, 1925.

9 Nather, K., Priesel, R., and Wagner, R. Die Beeinflussung des Blutzuckerspiegels durch Unterbindung der Ausführungsgänge der Bauchspeicheldrüse beim Hund, *Klin Wchnschr* **5** 932, 1926.

10 Jorns, G. Ueber das Verhalten der endokrinen Pankreasfunktion nach Unterbindung der Ausführungsgänge, *Klin Wchnschr* **5** 2434, 1926, Die Sklerose des Pankreas nach Unterbindung des Ausführungsganges und die Transplantation des sklerotischen Gewebes, *Beitr z klin Chir* **139** 325, 1927.

11 Alpern, D. E., and Besuglow, W. P. Beobachtungen ueber die Hyperfunktion des Inselapparates der Bauchspeicheldrüse, *Klin Wchnschr* **7** 586 (March 25) 1928.

12 Nather, K., Priesel, R., and Wagner, R. Die Beeinflussung des Blutzuckerspiegels durch Unterbindung der Ausführungsgänge der Bauchspeicheldrüse beim Hund, *Klin Wchnschr* **6** 2089, 1927.

13 Wohlgemuth, Julius, and Seo, T. Ueber experimentelle Erzeugung von chronischer Sympathicotomie beim Kaninchen, *Ztschr* **164** 271, 1925.

14 Galehr, O., Ladurner, P., and Unterrichter, L. Des Verhalten der Blutzuckerwerte nach Pankreasunterbindung, *Pflüger's Arch f d ges Physiol* **218** 477, 1928.

15 Jorns, G. Experimentelle und klinische Beiträge zur Pathologie der Langerhansschen Inseln des Pankreas, *Beitr z klin Chir* **146** 1, 1929.

*Site of Administration*—The subcutaneous route was painful when hypertonic concentrations were used. It concentrations of 5 and 10 per cent were used, the pressure of the great fluid volume made the animal restless and possibly excited. Thus another undesirable factor was introduced. The intraperitoneal administration of from 2.5 to 3 Gm of dextrose per kilogram of body weight was given serious trial. The absorption of dextrose is uniform and rapid. It may be influenced, however by operative procedures which damage the intact peritoneal surface. It also dehydrates the animal and thus may influence the blood sugar readings. Two of us (G de T and I J Seitz<sup>16</sup>) used this form of administration for more than a year. It was finally discontinued. Oral administration seems desirable, being the most physiologic entry of the dextrose into the body. The necessity of using the same concentration of dextrose for comparative curves is important. In the greater part of our experiments we used small repeated doses of sugar, the exact technic of which will be described later. Finally, the intravenous administration of dextrose, with the help of a Woodyatt pump was also used in our later experiments. As Woodyatt, Sansum and Wilder<sup>17</sup> pointed out, tolerance is more of a question of velocity, not so much of weight. The pump enabled us to administer accurate quantities of dextrose per hour. It also eliminated the variations of absorption from the site of administration.

*The Amount of Dextrose Ingested*—It was felt that for our work undertaken to demonstrate a possible increase of insulin output of the gland, smaller amounts should be used than is customary in sugar tolerance tests. Smaller amounts of dextrose cause a smaller increase in blood sugar and a change in the insulin output might be more easily detected. It was furthermore felt that a repeated dose of dextrose as suggested by Traugott<sup>18</sup> Staub<sup>19</sup> and Lennox,<sup>20</sup> would demonstrate the presence or increase of adequate insulin response much better than a single dose. Thus the amount of available insulin would be apparent not only by the height of the curve but by the rapidity of returning to the

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16 De Takats Geza, and Seitz Ira J. Unpublished data

17 Woodyatt, R. T., Sansum, W. D. and Wilder, R. M. Prolonged and Accurately Timed Intravenous Injections of Sugar. *J. A. M. A.* **45** 2057 (Dec 11) 1915

18 Traugott K. Ueber das Verhalten des Blutzuckerspiegels bei wiederholter und verschiedener Art enteraler Zuckerzufuhr und dessen Bedeutung für die Leberfunktion. *Klin. Wchnschr.* **1** 892 1922

19 Staub H. Ueber das Verhalten des Blutzuckers nach Verabfolgung kleiner Glucosemengen, *Ztschr. f. klin. Med.* **91** 44, 1921

20 Lennox W. Stimulation of the Sugar Regulating Mechanism as Shown by Duplicate Blood Sugar Curves. *J. Biol. Chem.* **73** 237 (March) 1927

normal level and by the posthyperglycemic hypoglycemia, but also by the flattening out of the second curve, as can also be observed in normal subjects

Noorden found that in light cases of diabetes, the first curve may show a normal return and that only the second curve reveals a typical diabetic abnormality. We have regularly been able to see the flattening out of the second curve in normal dogs, and feel that such a double sugar curve may give more information as to the response of the pancreas to hyperglycemia. So far as we could gather from the literature, Hamman and Hirschmann<sup>21</sup> were the first to use duplicate curves in man, long before the insulin era.

*Time of Fasting and Character of Previous Diet*—It has been repeatedly stated since Bang's initial observation,<sup>22</sup> that previous undernourishment or starvation will provoke an alimentary hyperglycemia, conversely, a curve taken a few hours after a meal is usually abnormally flat. In comparing curves, then, it must be postulated that the tolerance tests are run after the same period of fasting. According to Staub,<sup>19</sup> patients fed on a diet containing protein and fat showed definitely higher curves than patients on a diet containing carbohydrate. Experimental animals then must be kept on an identical diet during the entire experiment.

*Effect of Fear and Struggling*—One of the most important sources of error may be to compare subsequent tolerance curves in the animal and not consider the emotional effect of the stomach tube on the sugar curve. We show a fairly typical chart of three preoperative curves in the dog under identical conditions. We are convinced that the first alimentary hyperglycemia test is invariably too high, and that dogs should be trained to be in a relaxed, basal condition before tests of sugar tolerance are undertaken. The effect of the sympathetic nervous system on blood sugar is too well known to omit such a precaution. It can be readily seen that if in the case of dog 2 (chart 1) any therapeutic procedure had been carried out after the first curve, it would have led to the assumption that a great increase in tolerance took place. The gentle handling of the unflinching animal is equally important in the intravenous sugar tolerance tests. We have rejected several of these as the initial blood sugar was found to be too high. Cannon's students, who showed glycosuria after examination,<sup>23</sup> offer a striking example of emotional glycosuria.

21 Hamman, Louis, and Hirschmann, J. J. Effects upon the Blood Sugar of Repeated Ingestion of Dextrose, *Bull. Johns Hopkins Hosp.* 30: 306, 1919.

22 Bang, J. *Der Blutzucker*, Wiesbaden, 1913.

23 Cannon, W. B. *Bodily Changes in Pain, Hunger, Fear and Rage*, New York, D. Appleton & Company, 1918, p. 75.

It is true that the results of these experiments are not as conclusive as those of the experiments of other workers who have obtained more satisfactory results. The results of the present experiments are not as conclusive as those of other workers who have obtained more satisfactory results. The results of the present experiments are not as conclusive as those of other workers who have obtained more satisfactory results.

#### EFFECTS OF INSULIN TREATMENT

Healthy dogs were used in these experiments. They were accustomed to being fed on a schedule of twice a day at regular intervals. Food was omitted for a few days before the experiment was made. A sample of venous blood was taken after which 10 gm. of dextrose in 20 per cent solution was given by stomach tube. One hour later another identical dose of dextrose was given. Samples of blood were taken every fifteen minutes after each dose of dextrose for one hour so that altogether nine samples of blood were analyzed for sugar with the Folin-Wu method. At least two satisfactory curves were obtained before the operation. In some dogs from three to four preoperative determina-

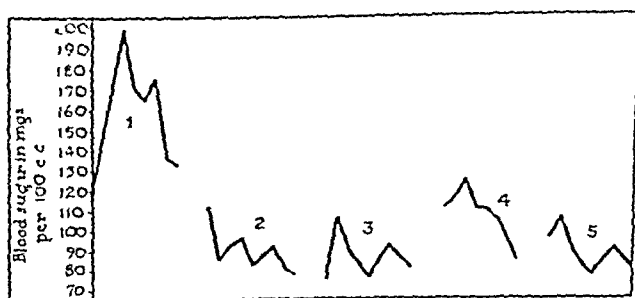


Chart 1—Effect of emotion feeding and starvation on oral sugar tolerance curves. Two grams of dextrose in 20 per cent solution was given by stomach tube twice, at one hour intervals. 1 stands for the emotional curve (dog struggled and was frightened), 2, dog was fed two hours previous to test, 3, dog was fed forty-two hours previous to test, 4 and 5 dogs were fed eighteen hours previous. The two latter are regarded as correct preoperative curves.

tions were made before a satisfactory curve could be obtained. The isolation of the tail of the pancreas was then undertaken as described in a previous communication.<sup>1</sup> In this series the electric cauter was used and the tail was wrapped up in omentum. We lost one dog under anesthesia but none following the operation.

After the animal recovered satisfactorily tolerance curves were determined once a month. In some dogs curves were obtained at closer intervals. In this series we have five dogs operated on for six months or longer. From a previous series ten dogs were carried over eighteen months but as they were chiefly used for histologic studies, we felt that the repeated pancreatic excisions and omental transplants would interfere with the sugar tolerance curves. They were not used. In two dogs of this series epinephrine hyperglycemia curves have been determined.

before and after the operation. After a sample of venous blood has been taken, 10 cc of a 1:10,000 solution of epinephrine has been injected intravenously. Samples of blood were taken at half hour intervals up to two hours.

Furthermore, in the same five dogs intravenous sugar tolerance tests have been performed with the Woodvatt pump. Unfortunately, determinations were not made before the operation, so that as a basis of normal tolerance the numerous determinations made by Woodvatt, Sumner and Wilder,<sup>1</sup> Felsner and Woodvatt<sup>2</sup> and Jordan<sup>3</sup> were utilized. From Woodvatt's original work it would seem that 0.9 Gm of dextrose per kilogram of body weight per hour is the maximal amount of sugar that can be injected without producing glycosuria. From the work of Woodvatt and Felsner elaborated by Jordan, it seems that by prolonging the intravenous administration of dextrose to several hours, more and more dextrose could be utilized. We have simply used 1, 1.5 and 2 Gm of dextrose per hour per kilogram of body weight to determine whether an increase of tolerance to this type of dextrose administration has taken place. Dextrose was injected in 5 and 10 per cent solutions, and urine was collected before and after the injection at a timed rate. The sugar, if present, was determined quantitatively by the Benedict method. Occasionally, blood sugar determinations were

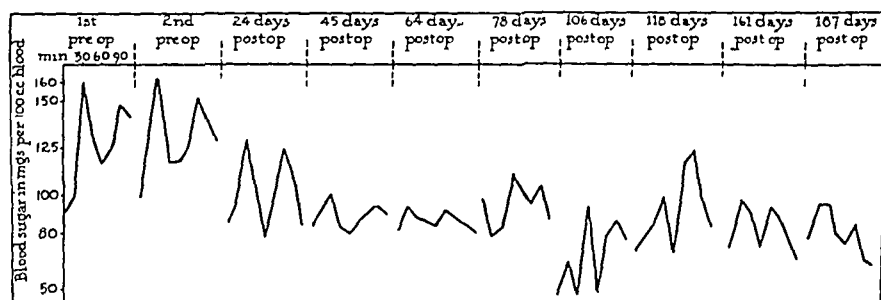


Chart 2—Double sugar tolerance curves obtained on dog 1, a white male, weighing 21 pounds (9.5 Kg). Two doses of 10 Gm of dextrose in 20 per cent solution were given by stomach tube at one hour intervals. The dog maintained his weight and was in good condition throughout the entire experiment.

made during the experiment. Finally, dogs were starved for two days after the blood sugar during fasting was taken, and a sample of blood was analyzed every morning. According to Mansfeld, this "Karenszypoglycæmie" was typical of the dogs operated on by his method.

## RESULTS

*Double Sugar Tolerance Curves*—Chart 2 illustrates the results obtained in dog 1. Following two correct preoperative curves, the post-operative curves show a marked fall in the blood sugar values during fasting together with a depression of the maximum rise following the

25 Felsner, Hannah, V., and Woodvatt, R. T. Studies on the Theory of Diabetes. Sugar Injection Curves in Dogs Under Intravenous Injection of Glucose at Lower Rates, *J Biol Chem* 60: 737, 1924.

26 Jordan, E. M. Effect of Injected Glucose on Tolerance, *Am J Physiol* 80: 441 (April) 1927.

ingestion of sugar. The lowest blood sugar during tasting was obtained one hundred and six days following operation namely, 48.7 mg per hundred cubic centimeters of blood. The average maximal rise in blood sugar was 73 per cent before the operation, the smallest post-operative rise was obtained on the sixty-fourth day namely, 18.75 per cent. On the seventy-eighth day the ingestion of 10 Gm of dextrose resulted in an initial hypoglycemia, followed by a rise in blood sugar. From here on the curves become steeper and less regular on the one hundred and sixth and one hundred and eighteenth days while the last two curves show a normal appearance. Even the last two curves as all others show a lower initial and maximal value in blood sugar than the preoperative curves. The maximal rise in blood sugar is 24.5 and 21.5 per cent in the last two curves. Also the posthyperglycemic hypoglycemia is marked as values of 66.6 and 57.1 mg per hundred cubic

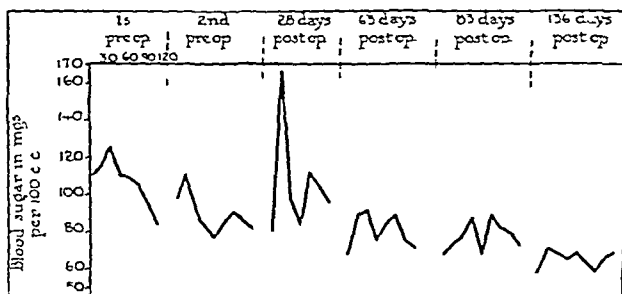


Chart 3—Double sugar tolerance curves obtained on dog 2, a brindle male, weighing 22 pounds (10 Kg). Ten grams of dextrose in 20 per cent solution was given at one hour intervals. Note the marked hypoglycemia following the double dose of dextrose before the operation. The high value in the first postoperative curve is open to question.

centimeters of blood were obtained on the one hundred and sixty-first and one hundred and eighty-seventh postoperative day. Throughout the whole period the dog maintained his initial weight of 21 pounds (9 Kg.).

Chart 3 illustrates the results obtained in dog 2. Following two preoperative curves which indicate a marked fall in blood sugar after a double dose of dextrose, four postoperative curves are available. The curve on the twenty-eighth day shows a sudden rise to 166.6 mg per hundred cubic centimeters of blood which reading may be questioned. Subsequent curves show a gradual decline in the values during tasting and the peaks. The lowest value during tasting of 59.3 mg per hundred cubic centimeters was obtained on the one hundred and thirty-sixth day. The average percental rise in blood sugar was 15.5 before the opera-



tion, the smallest rise after the operation was from 59.3 to 71.5 mg, a rise of 20.6 per cent. The dog weighed the same during the entire experiment, except for a temporary loss of 3 pounds (1.4 Kg) following the operation.

Chart 4 illustrates the results obtained in dog 3, a black and white male, weighing 25 pounds (11.3 Kg). The first preoperative curve was taken after forty-two hours of fasting, thus explaining the unusual rise following the administration of 10 Gm of dextrose. The second curve is quite flat. The lowest value during fasting was reached on the thirty-fifth postoperative day, namely, 51.2 mg per hundred cubic centimeters of blood. Subsequent curves do not show marked changes from the initial tolerance, although there is an instability of the sugar regulating mechanism on the one hundred and twenty-fourth day. The dog was in good shape and maintained his weight through the entire experiment.

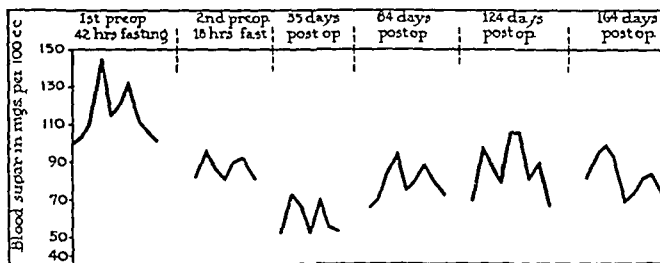


Chart 4—Double sugar tolerance curves of dog 3, a black and white male, weighing 25 pounds (11.3 Kg). Note the differences between the first and second preoperative curves, owing to different fasting periods before the feeding of dextrose. Ten grams of 20 per cent dextrose solution was given by stomach tube at one hour intervals. The dog looked sick and had running nose and eyes on the hundred and twenty-fourth day.

Chart 5 illustrates double sugar tolerance curves obtained on dog 4, a white male, weighing 30 pounds (13.6 Kg). One-half gram of dextrose per pound of body weight was given in 20 per cent solution at zero and one hour. A remarkable curve was obtained on the twenty-seventh day, when the sugar level of 80 mg per hundred cubic centimeters of blood fell to 57.1 mg as a posthyperglycemic reaction. The curve on the ninety-seventh day shows a definite diminution of tolerance and shows a characteristic diabetic curve. The dog was in good condition and showed no glycosuria. There was a loss in weight in the first few weeks but the dog regained his weight on the usual diet.

Chart 6 illustrates double sugar tolerance curves for dog 5, a male black bull dog weighing 26 pounds (11.8 Kg). One gram of dextrose

per pound of body weight was given in two doses at an hour's interval. The lowest level during fasting and the lowest peak was obtained on the thirtieth day. On the seventy-ninth day the curve still did not reach the preoperative level and the secondary rise was delayed as compared to the preoperative curves. The dog was in good condition and did not lose weight during the experiment.

*Epinephrine Curves*.—Ten cubic centimeters of a 1:10,000 solution of epinephrine was slowly injected intravenously before and twice after

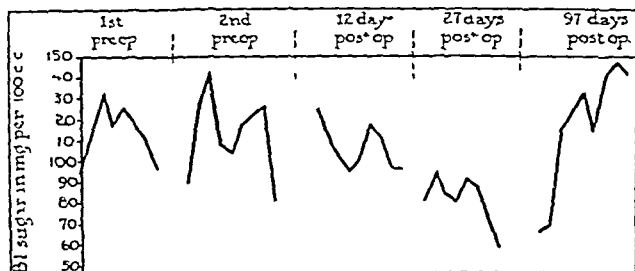


Chart 5—Double sugar tolerance curves obtained on dog 4, a white male weighing 30 pounds (13.6 Kg). One gram of dextrose per pound of body weight was administered in 20 per cent solution in two doses at one hour intervals. Note the marked increase and decrease in tolerance on the twenty-seventh and ninety-seventh days.

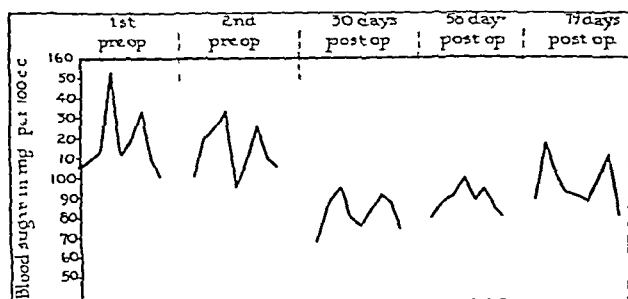


Chart 6—Double sugar tolerance curves obtained on dog 5, a black male bull dog, weighing 26 pounds (11.8 Kg). One gram of dextrose per pound of body weight was given in 20 per cent solution in two doses at one hour intervals. Note the gradual return to the original level although the last curve on the seventy-ninth day does not reach the original level.

the operation into two dogs. The curve of dog 2 showed a slight rise followed by a marked fall one and one-half hours after injection. Twenty-eight days after the operation a peculiar inversion of the curve occurred with a hypoglycemic value of 52.6 mg per hundred cubic centimeters of blood one hour after the injection followed by a sharp rise to 117.0 mg. One hundred and thirty-five days after the operation

the epinephrine curve was similar to the first one, with the exception of slightly lower values. Dog 3 showed a sharper rise in blood sugar than dog 2, and the curve did not drop under the initial level. Forty-seven days after the operation, a marked imbalance in carbohydrate regulation was brought about by the injection of epinephrine. The blood sugar fell and rose twice within two hours following the injection. During the same period the dextrose tolerance curves of this dog showed low values during fasting and slight rises. One hundred and sixty-three days after the operation, the epinephrine curve showed the usual form, except for a higher level, than the preoperative curve. One cannot be sure that this dog had not fasted too long before the first epinephrine curve was made, which would explain the low level of blood sugar during fasting. 57.1 mg per hundred cubic centimeters (chart 7)

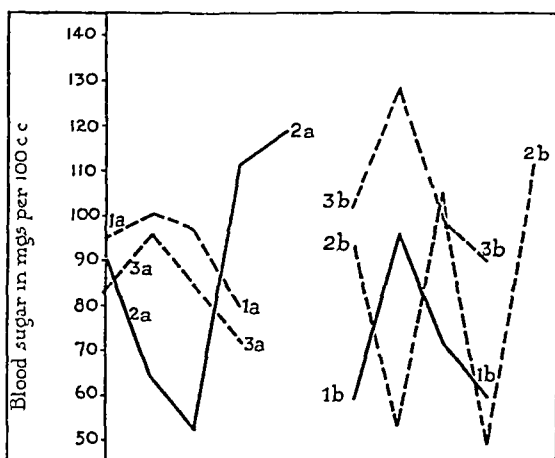


Chart 7—Epinephrine hyperglycemia on dogs 2 and 3, before and twice after the operation. Ten cubic centimeters of 1:10,000 solution of epinephrine was injected into the dogs, after eighteen hours of fasting. Samples of blood were taken before, one half, one and two hours after injection. 1 *a* indicates the curve taken before operation, 2 *a*, twenty-eight days after operation, 3 *a*, one hundred and thirty-five days after operation, 1 *b*, before operation, 2 *b*, forty-seven days after operation, 3 *b*, one hundred and sixty-three days after operation. Note the inversion of curves in both dogs, which return to normal in the second postoperative curve.

*Intravenous Sugar Tolerance Curves with Timed Rates*—The Woodyatt pump was used. One, 1.5 and 2 Gm of dextrose in 5 per cent solution were injected per kilogram of body weight for one hour. The urine was tested for sugar before the experiment and in the first twenty-four hour specimen following the injection. A few blood sugar determinations were also made.

The tolerance of dogs following this type of administration was as follows

TABLE 1—*Intravenous Sugar Tolerance Curves on Dogs, with Separation of the Tail of the Pancreas. Five per Cent Dextrose Solution was Given at a Timed Rate\**

Dog	Postoperative Day	Dose per Kilogram per Hour (Gm)	Glycosuria per Cent
1	103	2	
2	145	1.5	
3	147	2	0.3
4	130	1.5	
5	170	2	0.7
6	115	1	1.2
7	105	1.5	
8	165	2	1.1

\* The upper limit of tolerance in the normal dog was 0.9 Gm of dextrose per kilogram per hour (Woodratt Sansum and Wilder)

Dog 1, on the hundred and ninety-third postoperative day, received 2 Gm of dextrose per kilogram per hour which did not cause glycosuria.

Dog 2, on the hundred and forty-fifth postoperative day, received 1.5 Gm of dextrose which caused no glycosuria, 2 Gm of dextrose produced 0.3 per cent of sugar in the twenty-four hour specimen

Dog 3, on the one hundred and thirtieth postoperative day, showed no glycosuria with 1 and 1.5 Gm of dextrose per kilogram per hour. Two grams of dextrose produced a glycosuria of 0.7 per cent

Dog 4 on the hundred and fifteenth postoperative day, showed a glycosuria of 1.2 per cent following the intravenous injection of 1 Gm of dextrose per kilogram per hour

Dog 5, on the hundred and sixty-fifth postoperative day, showed no glycosuria with 1 and 1.5 Gm of dextrose. Two grams produced a glycosuria of 1.1 per cent

No preoperative determinations with this type of tolerance were made. The highest amount of dextrose that would not cause glycosuria in the normal dog was taken as 1 Gm per kilogram of body weight per hour, which is above the values given following numerous determinations of Woodratt Sansum and Wilder,<sup>17</sup> Woodratt and Felsher<sup>20</sup> and Jordan.<sup>26</sup>

*Blood Sugar Determinations on Fasting Dogs*—After eighteen hours of fasting a blood sugar determination was made, followed by two more determinations twenty-four and forty-eight hours later during which time the dogs did not receive anything but water. Table 2 illustrates our observations. The blood sugar level does not remain constant even in the normal dog, but may drop and rise within a limit of 20 mg per hundred cubic centimeters of blood. Numerous and careful determinations of Schwartz and Kemp<sup>27</sup> have given the same results. In all

27 Schwartz Karl and Kemp, Herwig. Ueber den normalen Blutzucker-gehalt beim Hunde und seine physiologische Schwankungen. Biochem Ztschr. 194 351 (Feb 7) 1928

dogs there was a sinking of the blood sugar values both at eighteen hours and at the end of another two days of starvation. The lowest figures were obtained from one to four months after the operation, after a while, a gradual rise took place, which approximately reached the preoperative values. The same wave of change in carbohydrate metabolism can be followed here as in our double sugar tolerance curves as has been observed by two of us in our unpublished intraperitoneal tolerance curves.<sup>10</sup> On dog 33 which had been used for our double sugar tolerance curves, only a preoperative and two subsequent starva-

TABLE 2—*The Effect of Starvation on the Blood Sugar Level Before and After Isolation of the Tail of the Pancreas\**

Dog	Fasting Period Hours	Pre operative Values Mg. per 100 Cc	Date of Oper- ation	Postoperative Values							
				9/21	10/25	11/17	12/1	12/27	1/11	1/30	2/19
26	21	101.5	7/27	90.9	75.2	79.4	85.1	71.0	71.5	80.0	95.1
	72	79.0		78.8	73.0	65.6	70.9	68.5	71.0	68.9	72.0
27	21	85.1	7/21	102.5	83.3	71.1	81.0	77.0	72.0	76.6	83.3
	72	79.3		81.6	58.3	66.6	70.0	60.0	68.0	67.1	68.0
28	21	90.7	8/23	76.9	81.0	68.9	71.4	78.0	71.5	72.5	71.0
	72	75.8		78.5	55.2	61.1	65.5	62.0	67.1	62.4	64.0
29	21	92.5	10/6			82.5	82.6	71.4		85.8	74.0
	72	80.0				59.0	60.0	66.0		66.6	66.0
30	24	89.2	12/1				90.2	73.0	75.4	72.5	74.5
	72	75.4					67.8	58.8	68.9	63.2	67.0
31	24	77.7	1/5						72.0	82.0	81.0
	72	76.7							71.0	64.5	65.0
32	21	77.0	1/5						78.6	78.1	76.0
	72	78.8							70.0	61.7	63.0
33	24	89.1	8/3			65.0					83.6
	72	70.2				39.5					81.2

\* This table illustrates the behavior of the blood sugar level after twenty-four and seventy-two hours of fasting. The dogs received as much water as they wanted and were not dehydrated as checked by hemoglobin determinations. One preoperative determination and several postoperative determinations were made. The lowest figures following three days of fasting were obtained around the third month. In dog 33 a typical hypoglycemia with extreme fatigue, restlessness and tremor developed on the ninety-fifth day. This was relieved within a few minutes by a dose of dextrose. The average lowest value was 37.5 mg per hundred cubic centimeters of blood.

tion curves were obtained. Ninety-five days after the operation, the blood sugar during fasting was 65 mg per hundred cubic centimeters of blood, twenty-four hours later, a reading of 41.3 mg and a day later of 39.5 mg of dextrose per hundred cubic centimeters of blood was made. The dog showed clinical symptoms of hypoglycemia, and was quickly relieved by dextrose. Two hundred and seventy-eight days later, the readings are close to the preoperative values. There was no change in the dog's weight and appearance during the whole experiment.

#### COMMENT

A study of our charts indicates that following the isolation of the tail of the pancreas in dogs a definite lowering of values during fasting

and a flattening of the curves took place in all five dogs. In dog 1 the lowest blood sugar level was encountered on the one hundred and sixth day, in dog 2 on the one hundred and thirty-sixth day, in dog 3 on the thirty-fifth day, in dog 4 on the twenty-seventh day and in dog 5 on the thirtieth day following operation. These blood sugar values during fasting are well below the lowest limit of normal and are also well below the preoperative blood sugar levels of the same dogs. Schwartz and Kemp in numerous determinations of the blood sugar of normal dogs during fasting found very small fluctuations during a period of several months.<sup>27</sup>

There was also a change in the character of the sugar tolerance curves. They became flatter and not only reached the fasting level within two hours after the double injection of sugar but frequently showed a posthyperglycemic dip.

The lower sugar values and flatter curves however did not persist at their almost hypoglycemic level but later showed a gradual rise. In dogs 1, 2 and 5 the level on the one hundred and eighty-seventh, one hundred and thirty-sixth and seventy-ninth day respectively was still decidedly below the preoperative values, in dog 3 the tolerance curve was similar to the preoperative curve on the one hundred and sixty-fourth day while dog 4 showed marked deterioration of the tolerance curve showing the aspect of a diabetic curve.

With the exception of dog 4 all the dogs permitted the injection of a larger than normal quantity of dextrose at timed rates without developing glycosuria. These determinations were made between the one hundred and fifteenth and the one hundred and ninety-third postoperative days.

The blood sugar determinations on dogs fasting for more than two days showed an inability or at least a decreased faculty for maintaining blood sugar at its physiologic level for a certain time after which a gradual return to preoperative values was observed.

The analysis of these observations must be undertaken with caution. It is true that hypoglycemia and flat tolerance curves immediately suggest an increased or uninhibited output of insulin from the pancreas. Following the case report of Wilder, Allan, Power and Robertson<sup>28</sup> some other cases of hyperinsulinism were reported in man. One case report spoke of dysinsulinism relieved after the removal of a small tumor in the pancreas.<sup>29</sup> Our histologic observations reported in a pre-

28 Wilder, R. M., Allan, F. N., Power, M. H. and Robertson, H. E. Carcinoma of the Islands of the Pancreas. *J. A. M. A.* **89** 348 (July 30) 1927.

29 Howland, G., Campbell, W. R., Maltby, F. I. and Robinson, W. L. Dysinsulinism, Convulsions and Coma Due to Islet Cell Tumor of the Pancreas with Operation and Cure. *J. A. M. A.* **93** 674 (Aug. 31) 1929.

vious paper, also indicate a regeneration and hypertrophy of insular epithelium following retention of pancreatic juice, yet hypoglycemia of hepatic and adrenal origin must first be excluded. The inability to store glycogen in the diseased liver diffusely invaded by an adenocarcinoma has been seen by Nadler and Wolfer,<sup>30</sup> in which case a clinical picture almost identical to that of hyperinsulinism has been personally observed by one of us (de Takats). In order to be sure that our dogs were not suffering from a lack of glycogen storage, a few glycogen determinations were made from biopsy material obtained under anesthesia produced by procaine hydrochloride and a barbitol derivative. From 4 to 6 per cent of glycogen was found in three of our dogs operated on at the time when they showed a low blood sugar level. One might even suspect, on the basis of Hetenyi's sugar determinations in tissues,<sup>31</sup> that an increased glycogen-fixation is present during insular hypoglycemia.

The reaction of the adrenals to this operation has been followed with great interest. The remarkable inversion of the epinephrine curve, which was observed at a certain period in two dogs, would indicate that the epinephrine hyperglycemia suddenly mobilized such an excess of insulin that the low blood sugar level of 52.6 mg. per hundred cubic centimeters of blood was reached half an hour after the injection. This low blood sugar in turn would mobilize endogenous epinephrine as has always been maintained by Cannon and this hyperglycemia would again call for insulin with a second dip to 47.9 mg. A remarkable imbalance of blood sugar regulation, which is temporary and is not observed in later epinephrine tests, suggests the possibility of changes in the nerve regulation of carbohydrate metabolism.

A number of workers maintain<sup>32</sup> that the interruption of sympathetic and parasympathetic fibers to the islets or to the liver produces changes in sugar tolerance. One is impressed with the abundance of nerve tissue in histologic sections of the pancreas. Some investigators might explain the results that we have observed on the basis of a partial denervating effect due to the separation of the tail from the body, but we believe that our observations are best explained by the histologic changes.

Omitting any tempting speculation, this much may be said of the effects of isolation of the tail of the pancreas on carbohydrate metabolism. A lowering of blood sugar values during fasting and an increase

30 Nadler, Walter H., and Wolfer, John A. Hepatogenic Hypoglycemia Associated with Primary Liver Cell Carcinoma, *Arch. Int. Med.* **44**: 700 (Nov) 1929.

31 Hetenyi, Geza. Experimentelle Untersuchungen über den Mechanismus der Insulin-Wirkung, *Ztschr. f. d. ges. exper. Med.* **45**: 440 1925.

32 Pollak, Leo. Der Mechanismus der alimentären Hyperglykämie, *Arch. f. exper. Path. u. Pharmacol.* **140**: 1 1929.

in sugar tolerance takes place. These changes occur from one to three months following the operation. Later these changes become less and less marked. In one dog preoperative tolerance was observed and in another a decrease in tolerance.

Several factors may be responsible for the return of the tolerance curves to normal or nearly normal. In the first place, our histologic studies as well as those of others have shown that the degree of sclerosis may later endanger the nutrition of the islets. A complete atrophy and sclerosis of the gland must sooner or later involve the islets. A type of diabetes may result as encountered following acute pancreatitis in man. This may have happened in dog 4. Hedon, Thirlow and Ivy and Farrell<sup>33</sup> observed a marked atrophy of the transplanted pancreas when it was not allowed to secrete externally. Jorns<sup>15</sup> laid great emphasis on the degree of sclerosis that may later endanger the function of the islets. In our earlier experiments we noted that a double silk ligature with complete severance of the body from the tail would set up more edema and later sclerosis of the gland than a division with the cautery which permitted drainage of pancreatic juice, and which resulted in much less atrophy and fibrosis than a ligature. In this respect, the careful work of Jorns, who could show an improvement in sugar tolerance far more readily following a single ligature of the duct than after complete evulsion and permanent severing of the duct, is remarkable.

This takes us back to the original suggestion of Mansteld who used only a single massive ligature around the body of the gland. This is bound to permit the reestablishment of the continuity of the duct, which seems to favor the persistence of the islands after the initial stimulus of a mild pancreatitis has subsided.

One must also consider the fact, repeatedly observed by us at explorations following the operation on the pancreas that not only the isolated tail of the pancreas, but the rest of the gland shows an edema and postoperative reaction. That an acute total pancreatitis with destruction of tissue may later lead to a hyperregeneration of islets must also be included in our possible interpretation of results. Allen<sup>34</sup> saw hypertrophic islets in his partial pancreatectomies. Fahr<sup>35</sup> performed gradual removal of the pancreas in several stages, and observed large islets as a response to increased functional activity of the remaining stump. Sprengel<sup>36</sup> reported a most instructive case, in which he saw the hemor-

33 Ivy, A. C. and Farrell, J. I. Contributions to the Physiology of the Pancreas. I. A Method for the Subcutaneous Autotransplantation of the Tail of the Pancreas. *Am J Physiol* **77** 474 (July) 1926.

34 Allen, F. M. *Glucosuria and Diabetes*. Boston: W. M. Leonard 1913.

35 Fahr, T. *Diabetes Studien*. Virenows Arch f path Anat **215** 247 1914.

36 Sprengel, H. Klinische und anatomische Untersuchungen an zu-geheilten Pankreastumektomien. *Beitr z klin Chir* **140** 117 1927.



rhagic edematous gland at operation and removed a large sequestrum of dead pancreatic tissue. Ten months later, when the patient died of intestinal obstruction the pancreas showed numerous and large islands and only a slight fibrosis in its midportion, as a remnant of previous destruction. We could find no case reports of increased sugar tolerance in cases of healed acute pancreatitis although shortly after the operation, low blood sugar values have been seen.<sup>1</sup>

It may be possible, then that in our dogs a hyperregeneration of lost islets took place, which gradually subsided.

Another cause of the slowly subsiding hypoglycemia in dogs may be the effort of compensation in a normal animal. It is reasonable to assume that if hypoglycemia would develop following increased or uninhibited secretion of insulin, the mechanism which normally regulates a steady blood sugar level would attempt to restore the physiologic level. The experiments of Langecker,<sup>27</sup> who found definitely hypertrophic adrenal glands following the prolonged administration of insulin are important in this connection. Gray and Feemster, who found compensatory hypertrophy and hypoplasia of the islets of a child born of a diabetic mother, described a hypertrophy of many medullary cells of the suprarenal glands.<sup>28</sup> The emergency theory of Cannon, McIver and Bliss,<sup>29</sup> could be applied perhaps to hypoglycemic states of longer duration. We have no proofs to offer for this suggestion. However, the tolerance curves in dog 1, which have been followed most closely would indicate that steep rises and falls are observed on the one hundred and sixth and one hundred and eighteenth postoperative days, as if an increased sympathetic tonus of the vegetative nervous system were present. Also the epinephrine curves show a fluctuating response to this drug. Wohlgenuth and his co-workers spoke of a sympathicotonia following ligation of the duct in rabbits, but believed this to be the result of diminished antagonistic action of the islet cells on the adrenals.

The increased capacity to utilize ingested carbohydrate is not unknown in pancreatic diseases of man. Bergmann believes that in acute edema of the pancreas, which precedes acute necrosis, a lowering of blood sugar may be observed as a result of islet stimulation.<sup>15</sup> Jorns showed a tolerance curve of a patient three days after operation for

37 Langecker, Hedwig. Der Einfluss chronischer Insulin-Zufuhr, auf die Nebennieren beim Kaninchen, *Arch f exper Path u Pharmacol* **134** 155, 1928.

38 Gray, S H, and Feemster, L C. Compensatory Hypertrophy and Hypoplasia of the Islands of Langerhans in the Pancreas of a Child Born of a Diabetic Mother, *Arch Path* **1** 348 (March) 1926.

39 Cannon, W B, McIver, M A, and Bliss, S W. Studies on the Conditions of Activity in Endocrine Glands. XIII. A Sympathetic and Adrenal Mechanism for Mobilizing Sugar in Hypoglycemia, *Am J Physiol* **69** 46, 1924.

acute pancreatic necrosis which showed a marked fall instead of a rise in the sugar level. Yet the blood sugar during fasting was 150 mg per hundred cubic centimeters of blood. One can hardly suppress the suggestion that the ingestion of sugar in such cases sets up a reflex which fixes glycogen in the liver instead of mobilizing it as it usually does. That this increase in glycogen fixation on a reflex basis may be the underlying cause of our low sugar levels and flat tolerance curves might also be considered without postulating any increase in insulin action.

The increase in glycogen fixation whether on a hormonal or on a nerve basis would be desirable in diabetes. One theory of diabetes that has not been shattered by the discovery of insulin is founded on increased glycogen mobilization as a result of hyperirritability of the sympathetic nervous system. Whichever theory of diabetes is favored a possible increase in glycogen fixation is worthy of a therapeutic attempt.

Such an operation in man should try to prevent a progressing sclerosis of the tail that would vitiate the initial results. In a case reported by one of us and Wilder<sup>40</sup> the gland was divided with the cautery to prevent too much retention and was wrapped in omentum with the hope of insuring better vascularization. Up to the present time—seven months after the operation—the improvement in sugar tolerance is still in progress.<sup>41</sup> We know far too little about the cause or causes of diabetes even to guess at the fate of regenerated islet cells. Would they be affected by the same agent that initially caused diabetes, or would their changed nerve supply protect them from inhibiting influences?

We have felt that the value of such an operation in man could be judged only by actual therapeutic attempts in juvenile diabetic patients whose power of regeneration is great, whose pancreas, particularly the blood vessels, is still intact and who show remarkably scarce histologic evidence of insular lesions. A study of such cases in patients operated on carried over a period of years will help to decide this problem.

Our experiments on animals are suggestive enough to justify further trial in man, especially since it has been shown that the operation can be performed safely. The problem of handling the pancreatic stumps will be discussed elsewhere. The fact that in the normal dog the low sugar values are not persistent does not mean that the diabetic patient

40 De Takats, Geza, and Wilder, Russell M. Isolation of the Tail of the Pancreas in a Diabetic Child. *I. A. M. A.* 93:606 (Aug. 24) 1929.

41 Since this article has gone to press another diabetic child has been operated on. Instead of using the division with the cautery, a strip of fascia lata was tied around the tail of the pancreas. Postoperative convalescence was smooth. Results of this operation will be published later.

might not be permanently benefited. While the performance of experiments on partially pancreatectomized dogs would seem tempting, we do not believe that the pancreatectomized dog is an ideal model for experiments for obtaining information concerning diabetes in man.

#### SUMMARY

1 In a series of five dogs, whose pancreas was divided with the electric cautery and then wrapped in omentum, double oral doses of sugar were given to test their sugar tolerance. Such tests repeated at intervals of from two to four weeks for several months showed a definite fall in blood sugar during fasting, a flattening of the tolerance curves and an increase in the posthypoglycemic hypoglycemia. In three of the five dogs, the lower levels still persisted at the conclusion of the experiment. One dog's values returned to normal, and one dog developed a definite decrease in tolerance.

2 Intravenous doses of dextrose at timed rates, carried out only once on each dog of this series showed that in four of five dogs a larger than normal amount of dextrose per hour per kilogram of body weight had to be given intravenously in order to produce glycosuria.

3 In dogs, fasting for from two to three days resulted in low amounts of blood sugar at a certain phase of the experiment, this phenomenon of "Karenyhypoglycemia of Mansfeld" was not permanent, and roughly followed the changes observed in the double sugar tolerance curves.

4 Blood sugar curves following the injection of epinephrine were determined three times in two animals, once before, once at the stage of lowest blood sugar values during fasting and once when the figures were returning toward normal values. A peculiar imbalance of carbohydrate regulation was reflected in these curves.

5 The correlation of these observations with our previous histologic studies would suggest the possibility that the mild pancreatitis set up by the stimulus of the operation results in a hypertrophy and hyperplasia of islet tissue, the functional activity of which is represented by the changes found in our present study. We are unable to say whether an actual increase in insulin output, a change in the secretory rate as a result of change in innervation or a functional liver block diminishing the outpour of glycogen is at play. Nor is it clear why these changes are not permanent. The possible causes for the return to the pre-operative status of the normal dog are discussed.

6 It is emphasized that these results can by no means indicate the possible effects of such an operation on man. This question can be decided only by operations on patients with diabetes.

## AUTOGENOUS FREE CARTILAGE TRANSPLANTED INTO JOINTS

AN EXPERIMENTAL STUDY \*

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AND

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Experimental investigation of the behavior of autogenous free cartilage in the joint space has been made difficult by the early attachment of such cartilage to the synovial membrane

Strangeways<sup>1</sup> expressed the view that articular cartilage derived its nutriment from the synovial fluid and that loose cartilaginous bodies not only survived in the joint cavities, but also increased in size. Such clinical evidence led Fisher<sup>2</sup> at about the same time to suggest the following two possibilities referable to the nutrition of cartilage: (1) that plasma flowed into the joint from the capillaries lying in the cancellous plates abutting on the calcified layer, or (2) that plasma flowing into the joint from the plexus of vessels lying beneath the synovia at the margin of the articular cartilage was the source of this nutrition. He also believed that cartilage cells free in a joint retained their vitality in almost every case and after a time actively proliferated.

Fisher<sup>2</sup> studied the behavior of cartilage in joints of the rabbit by chiseling off portions of cartilage which were freed in the joint. He stated

It was found in every case that the body acquired almost immediately an attachment to the synovial membrane that the latter surrounded it with a connective tissue sheath and that this sheath had the remarkable property of laying down new cartilage upon the surface of the original articular cartilage.

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\* Submitted for publication Nov. 23, 1929.

<sup>1</sup> From the Laboratory of Surgical Research and the Department of Pathology, the Lakeside Hospital and the Western Reserve University School of Medicine.

1. Strangeways, T. S. P. Observation on the Nutrition of Articular Cartilage. *Brit. M. J.* 1: 661 (May 15) 1920.

2. Fisher, A. G. T. A Study of Loose Bodies Composed of Cartilage or of Cartilage and Bone Occurring in Joints with Special Reference to Their Pathology and Etiology. *Brit. J. Surg.* 8: 493 (April) 1921.

Haas<sup>3</sup> studied the behavior of bone and cartilage transplants free in joints, hoping that by placing the fragments in a fenestrated rubber tube anchorage of the tissue to the synovial membrane might be prevented. In all of the twelve experiments, the contents of the tubes became adherent to the synovia which defeated the primary purpose of his investigation, namely, a study of the behavior of cartilage and bone without vascularization.

We cast about for some means whereby the phenomenon of adhesion and vascularization might be prevented in order that observations could be made on the response of cartilage when nourished as nearly as possible by the synovial fluid alone. After our work was completed, Pollock, McKenney and Blaisdell<sup>4</sup> reported certain experimental observations on the behavior of bone transplants, having used collodion membranes in about the same manner as we did with cartilage. Unfortunately none of their sacs remained intact. In view of these studies, as well as certain indeterminate work which has been done with cartilage cultures *in vitro*, we were led to believe that pieces of cartilage might be placed in some dialyzable membrane which would permit nourishment of the tissue by synovial fluid alone, without vascularization from the synovia, using at the same time a substance that would not act as a chemical irritant to the tissues.

The conclusions referable to the behavior of cartilage free in the joint space previous to this time have been largely theoretical deductions drawn from pathologic material removed from the human joint at operation or autopsy.

#### EXPERIMENTAL PROCEDURE

Thirteen dogs, between 4 and 8 months of age, were used for this investigation. Two pieces of cartilage were removed from the right knee and introduced into the joint cavity of the left knee of each animal.

Drop ether anesthesia was used, and the skin over the inner aspect of each knee was shaved and prepared with alcohol and mercuric chloride. The cartilage was removed by shaving the joint surface of the lateral eminence of the lower portion of the articular surface of each femur. In most instances, the entire thickness of the articular cartilage, together with a thin layer of the subchondral spongiosa, was obtained. Each specimen of cartilage was approximately 6 mm long with a maximum width of 3 mm. The thickness varied, but averaged between 2 and 3 mm. In some of the animals only a single specimen was taken, as recorded in the protocol.

One specimen of cartilage was enclosed in a collodion sac and is a control; the other cartilage was introduced uncovered into the joint cavity.

<sup>3</sup> HARRIS S. L. The Transplantation of Bone into Joints. *Arch. Surg.* **13** 426 (Sept.) 1926.

<sup>4</sup> POLLOCK W. E., MCKENNEY P. W. and BLAISDELL F. E. The Viability of Transplanted Bone. An Experimental Study. *Arch. Surg.* **18** 607 (Feb.) 1929.

Collodion sacs were prepared by inserting the end of a glass tube into one half of an ordinary small gelatin capsule and dipping it into an 8 per cent solution of collodion. The collodion was allowed to dry in the air for five minutes and was then redipped. While the collodion was drying the tube was twirled to prevent an uneven coating. Five minutes after the second dipping the tubes were immersed in water and the collodion coated capsule was removed by circling the tube with a sharp knife and blowing on the open end. The gelatin was then dissolved and washed out of the sac with warm water. The sacs were stored in the refrigerator in physiologic solution of sodium chloride. Just before being used these sacs were washed in 70 per cent alcohol and rinsed with sterile saline solution. The sac was then filled with saline solution the sliver of cartilage inserted and the sac tied with silk, then dried and dipped in ether and the entire end including the silk tie smeared with collodion.

All sacs were tested for defects before being used. It was found that such a sac permitted diffusion of inorganic salts in solution but did not allow passage of the protein molecule. The dialysate of blood serum through such a sac was found to be negative for protein or protein split products by the biuret and Heller's ring test. At the end of varying periods of time the left knee joint of each animal was reopened and both fragments of cartilage were removed. Each piece of cartilage including the collodion covering of the one was fixed in formaldehyde, sectioned serially and stained with hematoxylin and eosin.

#### PROTOCOLS

**PROTOCOL 1**—Three specimens of cartilage were taken from the right knee of dog 1, weighing 54 Kg. One was fixed in formaldehyde immediately and the other two were introduced into the cavity of the dog's left knee joint. At the end of seven days the dog died of pneumonia. The left knee was opened, the wound had healed by first intention and the synovia was smooth and free from inflammation. The encapsulated as well as the unencapsulated piece of cartilage was found to be free from adhesions and the two lay in the posterior joint space.

**Histologic Observations**—Control Specimen of Cartilage. Sections included the entire thickness of the joint cartilage with a lower margin of attached subchondral spongiosa. The cartilage had a homogeneous faintly basophilic matrix. The cells just below the articular surface were spindle-shaped and disposed parallel to the surface. Deeper in the cartilage they were spherical and larger and as the zone of provisional calcification was approached they showed some tendency to be arranged in columns. The cells occurred in small clusters. The nuclei were round, and the cells filled their lacunae. There was a zone around the lacunae in the deeper portion of the cartilage in which the matrix took a more deeply basophilic stain. The zone of provisional calcification was narrow and incomplete with occasional vascular loops penetrating it from the marrow. The trabeculae of the primary spongiosa were heavy and thickly disposed.

**Unencapsulated Cartilage**. This was removed seven days after its implantation in the left knee joint. Sections of cartilage included a narrow zone of primary spongiosa. The entire specimen was encased in a loose capsule of fibrous connective tissue. The superficial zone of cartilage showed considerable absorption of matrix with exposure of the fibrils. The exposed fibrils of the cartilage blended indistinguishably with the covering fibrous connective tissue. The disposition, number and size of cartilage cells did not appear to be changed. The articular zone of the matrix was acidophilic and the basophilic cell areolae of the deeper cartilage were paler than those observed in the control. The zone of

provisional calcification showed no change. There were two shallow knife wounds which represented operative artefacts. These were both filled by fibrous connective tissue which appeared to be an ingrowth from the fibrous capsule of the implant.

**Encapsulated Cartilage.** The specimen of cartilage (fig 1) was removed seven days after its encapsulation and implantation in the knee joint. The collodion sac appeared to be intact throughout. The surface of the cartilage showed a narrow zone of granular basophilic necrosis. There was no connective tissue covering beneath the necrotic zone. There was some absorption of matrix with exposure of the fibrils. The entire specimen showed some loss in basophilic staining properties, and there was a complete disappearance of the basophilic cell areolae. The cartilage cells showed various stages of degenerative changes, although most of them appeared normal. The degenerative changes were

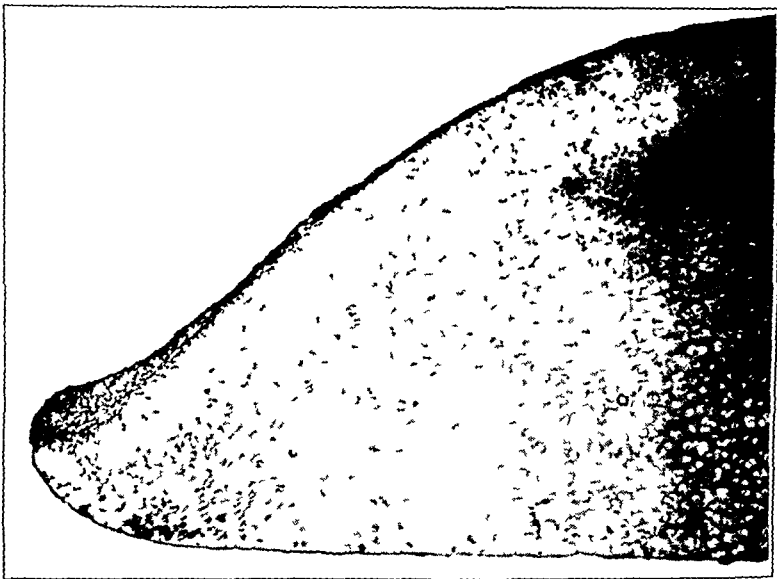


Fig 1—Specimen of cartilage from dog 1. The cartilage was enclosed in a collodion sac and implanted in the joint cavity for seven days. The sac remained intact.

manifested by a shrinkage of cells within their lacunae. In some instances, the nuclei were pyknotic, and a considerable number of lacunae appeared empty. The cartilage cells in the deeper layers showed no change other than a loss of cell areolae. One small knife wound in this piece of cartilage gaped and showed no healing.

**PROTOCOL 2**—Two pieces of cartilage were taken from the right knee of dog 5, weighing 62 Kg, and inserted into the cavity of the left knee joint. One was unencapsulated and the other was enclosed in a collodion sac. After twenty-two days, the knee joint was opened and both cartilages were removed. The encapsulated cartilage was found to be incorporated in the wound just beneath the synovia. It was firmly attached by fibrous adhesions. The unencapsulated cartilage was free in the joint space. The synovia was smooth and there was no evidence of inflammation.

*Histologic Observations*—Unencapsulated Cartilage The unencapsulated specimen of cartilage including a portion of the subchondral osseous lamella was enclosed in a thin fibrous connective tissue capsule. The cartilage showed a superficial lacunar absorption of matrix with superficial exposure of fibrils and invasion by the surrounding fibrous connective tissue. The cells filled their lacunae and showed no degenerative changes, and the basophilic areolae were well marked. The zone of provisional calcification and underlying osseous lamella showed no change.

Encapsulated Cartilage The collodion sac contained several small defects through which fine strands of fibrous connective tissue extended. At the ends of the specimen the exposed fibrils merged indistinguishably with a thin layer of fibrous connective tissue which completely covered the specimen and filled in the marrow spaces between the trabeculae of the primary spongiosa. There was some diminution in the staining intensity of the cell areolae. The cartilage cells themselves showed no changes.

PROTOCOL 3—A single piece of cartilage was taken from the right knee of dog 53, weighing 23 Kg. and enclosed in a collodion sac and introduced into the joint cavity of the left knee. After twenty-two days, the left knee was reopened and the encapsulated cartilage was found free in the joint cavity.

*Histologic Observations*—There was no evidence of any defect in the sac. The thin ends of the specimen were the seat of granular basophilic necrosis, and the cells in the superficial layer of the cartilage showed an unusual degree of flattening, but there was no apparent absorption of matrix nor exposure of fibrils. The cartilage appeared to have shrunk. This appearance was due to the flattening of cartilage cells throughout a fairly wide peripheral zone. Deeper in the cartilage, the cells were large, spherical or biscuit-shaped and filled their lacunae. There was some reduction in basophilic staining property, and the cell areolae were relatively pale.

PROTOCOL 4—A piece of cartilage enclosed in a collodion sac was introduced into the cavity of the left knee of dog 33, weighing 35 Kg. After twenty-five days, the knee was reopened, and the encapsulated cartilage was found free in the joint space.

*Histologic Observations*—The sac was intact, and the sliver of cartilage was rounded off to fit the space within the sac. The cartilage (fig 2) appeared in an excellent state of preservation, and the basophilic cell areolae were pale and did not offer much contrast to the neutrophilic matrix. There was no evidence of fibrous connective tissue proliferation within the sac.

PROTOCOL 5—Two specimens of cartilage were removed from the right knee of dog 4, weighing 41 Kg., and introduced into the left knee. After twenty-eight days the joint was reopened, and neither the encapsulated nor the unencapsulated specimen could be identified. The joint space was distended with a viscid purulent exudate and the synovial surface was covered with fibrinous exudate.

PROTOCOL 6—Two pieces of cartilage were introduced into the joint cavity of the left knee of dog 99, weighing 62 Kg. The knee was reopened after twenty-eight days. The wound had healed by first intention. The specimen enclosed in a collodion sac was free in the joint space. The unencapsulated specimen was firmly attached to the synovia.

*Histologic Observations*—Unencapsulated Cartilage The cartilage occupied the center of a synovial projection and was covered with a thick layer of fibrous



connective tissue which showed abundant vascularization. The cartilage showed lacunar absorption of the matrix from the surface both from above and from below. There was extensive vascularization of the cartilage. The matrix, however, appeared homogeneous, and the cartilage cells showed no change. There was some loss in basophilic staining properties.

**Encapsulated Cartilage.** The sac was not intact, and at one end there was a narrow pedicle of fibrous connective tissue extending through a defect in the sac and becoming continuous with a thin fibrous layer that covered the cartilage. The cartilage itself appeared fibrous, and with high magnification the cells were elongated and spindle shaped.

**PROTOCOL 7**—One specimen of cartilage was enclosed in a collodion sac and introduced into the joint cavity of the left knee of dog 39, weighing 5.2 Kg.

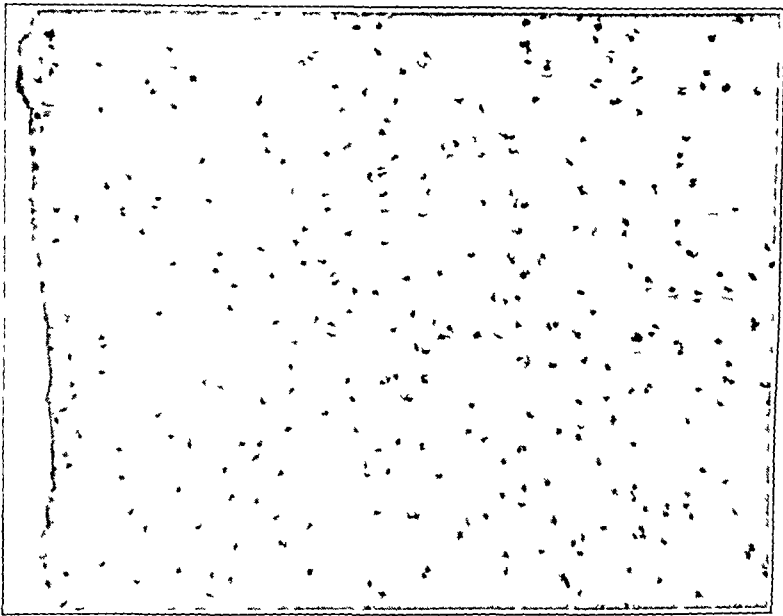


Fig 2—Specimen of cartilage from dog 33. The cartilage remained twenty-five days in the joint cavity and was enclosed in an intact collodion sac.

The left knee was reopened after thirty-two days. The wound had healed, but there was marked edema of the subcutaneous tissue, and the joint cavity was distended with cloudy fluid. The tip of the sac enclosing the cartilage was found to be attached to the synovia.

**Histologic Observations**—There was a large defect in one end of the sac with a band of young fibrous connective tissue extending through the sac. The cartilage itself had entirely disappeared leaving only the subchondral osseous lamella and a few trabeculae of the primary spongiosa. There was a small amount of exudate within the sac consisting of polymorphonuclear leukocytes and fibrin.

**PROTOCOL 8**—A single specimen of cartilage was removed from the right knee of dog 48, enclosed in a collodion sac and introduced into the joint cavity of the left knee. The joint was reopened after thirty-two days, and the encapsulated cartilage was found attached to the hypertrophic synovia.

*Histologic Observations* (fig 3)—There were several small defects in the sac through which slender bands of fibrous connective tissue extended to become continuous with a thin fibrous capsule that enclosed the cartilage. There was a slight degree of matrix absorption along the superficial surface, and the surrounding fibrous connective tissue was vascularized. The cartilage itself showed no vascularization. The cartilage cells filled their lacunae, and at the narrow ends of the specimens and for a short distance beneath the surface the lacunae were connected with one another by a system of canaliculi (figs 3 and 4). These canaliculi were readily identified since they took a deeper basophilic stain than the surrounding matrix. Deeper in the cartilage, the matrix was homogeneous, and there was no apparent communication between lacunae. In several slides, the canaliculi extended to the surface of the cartilage and apparently opened into the intercellular spaces of the fibrous connective tissue covering.



Fig 3—Specimen of cartilage from dog 48 showing a defect in the collodion sac and the formation of interlacunar canaliculi

PROTOCOL 9—A single specimen of cartilage was removed from dog 38, weighing 35 Kg, enclosed in a collodion sac and introduced into the cavity of the left knee. After thirty-two days the left knee was reopened and the encapsulated cartilage was found free and unattached in the anterior joint space.

*Histologic Observations* (fig 5)—Sections showed the sac to be intact, and the cartilage appeared to be in an excellent state of preservation. The cells were small but filled their lacunae except at the narrow ends of the specimen where the lacunae appeared vesicular and either were empty or contained only a pyknotic remnant of the cartilage cell. The matrix was uniformly acidophilic, and the cellular stroma were lost. Here as in the encapsulated specimen from dog 48 a system of canaliculi connected the lacunae. In this specimen the canaliculi were not limited to the periphery and ends but were seen throughout almost the entire matrix.

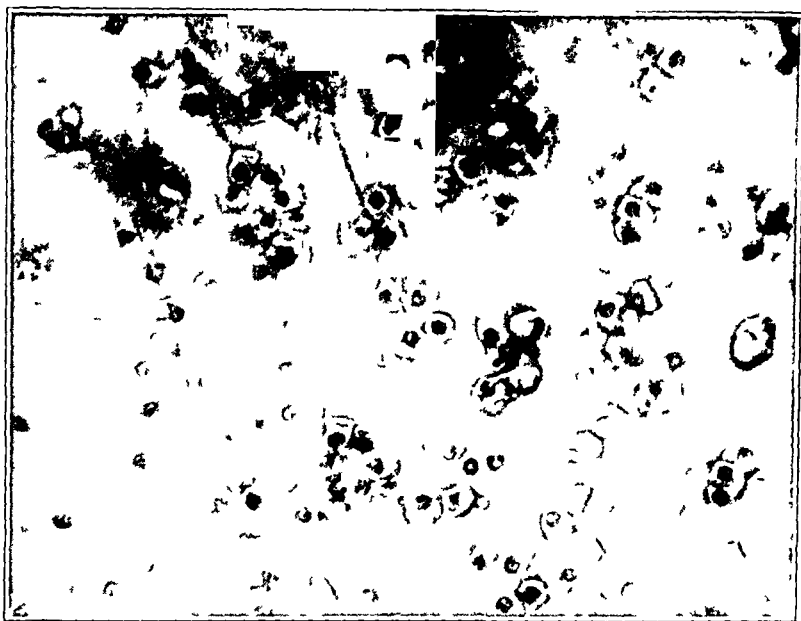


Fig 4—High power magnification of interlacunar canaliculi Specimen of cartilage shown in figure 3



Fig 5—High power magnification of cartilage from dog 38 showing interlacunar canaliculi

**Protocol 10**—Because of the thinness of the articular cartilage, three small shavings of cartilage were removed from the joint space of the right femur of dog 32 weighing 5.45 Kg. The fragments were all small, and were enclosed in a sac which was introduced into the left knee. After thirty-seven days, the sac was removed. There was some excess of synovial fluid, and the synovia was covered with irritable villous granulation. The sac was grossly intact and was embedded in a pocket in these granulations.

*Histologic Observations*—Sections showed the subchondral spongiosa entirely denuded of cartilage. There were many small defects in the sac which contained purulent exudate.

**Protocol 11**—Three pieces of cartilage were removed from the articular surface of the right femur of dog 96 weighing 7.2 Kg. One was taken for histologic examination of normal cartilage, one was introduced without covering, and the other was enclosed in a collodion sac and placed in the left knee joint. At the end of fifty-two days the left knee was reopened and showed no evidence of inflammation. The encapsulated and nonencapsulated specimens were adherent to one another and to the synovia in the intercondylar fossa.

*Histologic Observations*—Control Specimen of Cartilage. The control specimen had an appearance essentially identical with that of the control specimen described in protocol 1 (dog 1).

**Unencapsulated Cartilage** The unencapsulated specimen of cartilage was surrounded by a fibrous connective tissue capsule which was continued as a vascularized pedicle from one end. The cartilage showed considerable peripheral matrix absorption and fibrous connective tissue replacement. The matrix was fibrillar rather than homogeneous, and the deeper cartilage cells appeared well preserved, and filled their lacunae, which were rounded. Toward the surface, these lacunae were elongated and disposed parallel to it.

**Encapsulated Cartilage** The collodion sac had many small defects with extension of the surrounding fibrous connective tissue into the sac and around the enclosed cartilage. The cartilage was almost entirely replaced by fibrous connective tissue and showed vascularization. The lacunae throughout most of the specimen were connected with one another by small canaliculi similar to those previously described.

**Protocol 12**—Two pieces of cartilage were removed from dog 97, weighing 6 Kg., and one was placed in a collodion sac. Both specimens were inserted into the left knee joint. After eighty-four days, the left knee was reopened, and both specimens were found to be adherent to the synovia by fine fibrous adhesions.

*Histologic Observations*—Unencapsulated Cartilage. The specimen included a generous amount of attached subchondral spongiosa. The cartilage was vascularized and enclosed in a thick cushion of fibrous connective tissue. The matrix was homogeneous and took acidophilic stain.

**Encapsulated Cartilage** There were large defects in the collodion sac, and the entire specimen of cartilage was ensheathed in fibrous connective tissue, which had replaced the superficial zone of the cartilage. The matrix was homogeneous and showed a loss of basophilic staining properties. The cartilage cells appeared well preserved and filled their lacunae. The lacunae at the ends and in the superficial portions of the cartilage were seen to be connected by a network of fine canaliculi.

**Protocol 13**—The articular cartilage from dog 98 weighing 7.4 Kg. was thin, and it was possible to remove only a thin shiver of cartilage which was enclosed in a collodion sac and introduced into the cavity of the left knee. At the end of

194 days, the left knee was reopened. The joint fluid was clear, and the synovia was smooth, except at the site of the scar of the previous operation. There was no evidence of the sac or the cartilage.

#### COMMENT

Four of the thirteen collodion sacs introduced into the knee joints remained intact. In six sacs there were defects, and four of these six were attached to the synovia by vascularized pedicles of fibrous connective tissue while two were free in the joint cavity and showed no vascularization. In three instances, both sac and cartilage had partially or entirely disappeared in the purulent exudate within the joint cavity.

The four specimens of cartilage enclosed in sacs which remained intact were removed from the joint cavity after seven, twenty-two, twenty-five and thirty-two days, respectively. These pieces of cartilage were all well preserved and contained what appeared to be living cells (figs 1 and 2). The contour of the cartilage had rounded and become adapted to the shape of the sac, so that there was no space between sac and cartilage. There was a narrow superficial zone in each cartilage which was acellular, and the matrix of this zone appeared finely granular and faintly basophilic. Generally, there was a loss of the basophilic staining property of the matrix, and the deeply basophilic cell areolae had entirely disappeared. The cells, for the most part, filled their lacunae and appeared unchanged. However, at the narrow ends of the specimen and for a short distance beneath the surface many of the cells had shrunk away from their lacunae, and the nuclei were in many cases pyknotic. A few lacunae were empty, and the cell had entirely disappeared. There were two essential differences between the unattached cartilage free in the joint cavity and enclosed in an intact sac and the unattached cartilage free in the joint cavity and enclosed in a defective sac that admitted the passage of whole synovial fluid. In the former, the cartilage cells appeared concentrated, as though the entire specimen had become somewhat shrunk, and yet exposure of fibrils was relatively insignificant. In the latter, varying degrees of matrix absorption had taken place, but there was no apparent shrinking or concentration of cells in the still recognizable cartilage. The other difference was the entire lack of cell proliferation within the intact sacs (figs 1 and 2). Knife wounds in these pieces of cartilage showed no evidence of healing, and there was no capsule of fibrous connective tissue interposed between sac and cartilage. In the latter, there was proliferation of fibrous connective tissue to fill the interstices within the sac (fig 3) and to heal the knife wounds.

In those specimens of cartilage enclosed in sacs which had not remained intact the changes were not uniform and did not show a consistent relationship to the time during which they had remained in the joint cavity. Absorption of the matrix so that the fibrils were recognizable was fairly constant. Fibrous metaplasia of cartilage was a characteristic change and appeared to proceed from the surface in toward the subchondral osseous lamella which was in most instances attached. In the deeper portions of the cartilage the cells were round or oval and occupied definite lacunae in a hyaline matrix. As the surface was approached these cells were more and more elongated and the matrix appeared more fibrillar and the transition from cartilage to the fibrous connective tissue covering was so gradual that no sharp line of demarcation was seen. This fibrous metaplasia constituted an interesting distinction between cartilage which had survived in an intact sac and cartilage which had survived in a sac permitting free access to synovial fluid. In the former there was more "Demaskierung" but no metaplasia, while in the latter metaplasia was a characteristic change. If the change from cartilage to fibrous connective tissue is dedifferentiation, it should have occurred in both instances.

In a number of specimens of cartilage which had been in defective sacs, a fine network of interlacunar canaliculi was seen (figs 3-4 and 5). In some of the specimens, this system was apparent only at the narrow ends and beneath the surface while in others the entire piece of cartilage was traversed by the canaliculi. They extended between the cell lacunae and also communicated with the surface.

Such a system of interlacunar canaliculi has been observed in the cartilage of various of the invertebrates. Dahlgren and Kepner<sup>5</sup> noted that in the cartilage of squid and other invertebrates there is a system of communicating passages between cell lacunae through which cytoplasmic processes of the cells extend. These cell processes they believe provide for the passage of food and other materials. Cajal is cited by Bailey<sup>6</sup> as having observed a system of fine white lines connecting the cells of the costal cartilage of young dogs. Hammar<sup>7</sup> stated that he observed unquestionable interlacunar communication only in the superficial zone of the articular cartilage and although many investigators have reported the finding of interlacunar passages he was unable to determine whether they are preformed or artefact.

<sup>5</sup> Dahlgren, Uric and Kepner, W. A. A Textbook of the Principles of Animal Histology. New York: The Macmillan Company, 1908.

<sup>6</sup> Bailey, F. R. A Textbook of Histology, ed. 6, New York, William Wood & Company, 1920.

<sup>7</sup> Hammar, J. A. Ueber den feineren Bau der Gelenke. Arch. u. mikr. Anat. 43: 813, 1894.

Solger<sup>8</sup> observed this structural character of hyaline cartilage and believed it to be an artefact of fixation. Wolters<sup>9</sup> believed the communication to be preformed. Several conditions led us to the opinion that these canaliculi were actual and not artefact. The manner in which they widened and became funicular as they approached cell lacunae did not appear consistent with the conception of artefact (fig 5). Under low magnification, this system of canaliculi appeared to form an intercommunicating network (fig 3), but with high magnification it was seen that the canaliculi did not communicate with one another, except through cell lacunae (fig 5). They extended between single cartilage cells or groups of cells and occasionally reached the surface. Their distribution bore no relation to the long axis of the fibrils (fig 3), and if their appearance was due to dehydration and shrinkage we should expect that there would have been a definite relationship between the long axis of the interlacunar channels and the direction of the matrix fibrils.

In no instance was this canalicular system seen in normal joint cartilage, nor was it seen constantly in the specimens of cartilage enclosed in collodion sacs. It seems entirely possible that the patency of the canaliculi depended on the degree of elasticity of the matrix and that they became visible incidental to matrix absorption. That matrix absorption occurred was indicated by the concentration of cartilage cells.

#### SUMMARY

Articular cartilage will survive as long as thirty-two days, nourished only by the diffusible elements of the synovial fluid. Unattached, nonvascularized cartilage in direct contact with synovial fluid shows superficial fibrous connective tissue proliferation, while cartilage enclosed in a collodion sac and accessible only to the diffusible elements of the synovial fluid shows no cell proliferation. The demonstration of fibrous connective tissue proliferation in unattached, nonvascularized tissue in the joint space offers an explanation for the spontaneous production of and accretion to joint-mice. A system of interlacunar canaliculi adequate to provide for circulation of fluids in the matrix of articular cartilage is demonstrated.

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8 Solger, B. Ueber Schrumpfungerscheinungen am hyalinen Knorpelgewebe des Menschen und deren Beziehungen zu den Fibrillen, *Arch f mikr Anat* **31** 303, 1888.

9 Wolters, M. Zur Kenntnis der Grundsubstanz und der Säftbahnen des Knorpels, *Arch f mikr Anat* **37** 492, **38** 618, 1891.

# THE CAUSE OF DEATH IN UNCOMPLICATED HIGH INTESTINAL OBSTRUCTION

EXPERIMENTAL EVIDENCE TO SHOW THAT DEATH IS DUE NOT TO  
TOXEMIA, BUT TO LOSS OF DIGESTIVE FLUIDS AND SALTS\*

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AND  
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The cause of death in all types of intestinal obstruction has been so long and so unanimously ascribed to toxemia that the work of a small group who maintain that toxemia is not important in simple high occlusion has been rather generally disregarded. This group comprises the following investigators:

1 Hartwell and Hoguet,<sup>1</sup> who in 1912 first called attention to the life-saving properties of salt solution. They believed that its physiologic effect was in the prevention of the dehydration, which they considered to be the chief lethal factor.

2 Gamble and McIver,<sup>2</sup> who believed that in these cases death is due primarily to the loss of the electrolytes sodium and chlorine, with secondary inability of the tissues to maintain their normal fluid content.

3 White and Bridge,<sup>3</sup> who pointed out that since salt is lost from all the viscera, muscles and skin, as well as from the blood, by vomiting, the chloride ion cannot have the toxin-neutralizing effect ascribed to it by Haden and Orr<sup>4</sup> and other recent writers, e g, Phillips and Stowe.<sup>5</sup>

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\* Submitted for publication, Dec 9, 1929.

\* From the Surgical Services, Massachusetts General Hospital, and the Surgical Research Laboratories, Harvard Medical School.

1 Hartwell, J A, and Hoguet, J P. Experimental Intestinal Obstruction in Dogs, with Special Reference to the Cause of Death and the Treatment by Large Amounts of Normal Saline Solution, *J A M A* **59** 82 (July 13) 1912.

2 Gamble, J L, and McIver, M A. Body Fluid Changes Due to Upper Intestinal Obstruction, *J A M A* **91** 1589 (Nov 24) 1928.

3 White, J C, and Bridge, E M. Loss of Chloride and Water from the Tissues and Blood in Acute High Intestinal Obstruction, *Boston M & S J* **196** 893 (June 2) 1927.

4 Haden, R L, and Orr, T G. The Effect of Sodium Chloride on the Chemical Changes in the Blood of the Dog After Pyloric and Intestinal Obstruction, *J Exper Med* **38** 55 (July) 1923. These investigators now believe that the neutralization theory is untenable, but they still claim that toxemia is the important factor in causing death in this type of case (Chemical Factors in the Toxemia of Intestinal Obstruction, *J A M A* **91** 1529 [Nov 17] 1928).

5 Phillips, K, and Stowe, W P. Intestinal Obstruction and Septic Invasion of the Peritoneum, *Arch Int Med* **44** 543 (Oct) 1929.



4 Wilkie,<sup>6</sup> who in 1913 wrote "Simple obstruction of the intestinal lumen must be clearly distinguished from strangulation" He pointed out further, that when an obstruction was placed between the upper secretory part of the intestine and the lower absorptive part, the resulting condition was due to loss of the vomited secretions, and not so much, if at all, to toxemia

More recently, Foster and Hausler,<sup>7</sup> as well as Gatch, Trussler and Ayres,<sup>8</sup> divided intestinal obstruction into two main groups (1) simple occlusion of the lumen of the upper small intestine without interference with its blood supply—no toxemia, (2) "strangulation obstruction," with impairment of circulation, in which toxemia is marked, as shown by physiologic and biochemical experiments

One of us (J C W<sup>9</sup>) reported further experimental and clinical evidence in support of the classification In the first group, toxemia is not important if the occlusion is high enough for the obstructed bowel to empty itself freely by vomiting, since then it does not become distended to the point of losing its normal blood supply In such cases, as Wilkie<sup>6</sup> showed, even if toxins are present in the obstructed contents, they are not absorbed by the normal intestinal mucosa to any appreciable extent<sup>10</sup> Life can be prolonged many days in these cases simply by the replacement of sodium chloride and water However, if the loss of these substances in the obstructed secretions is not compensated, experimental animals and human beings die when the chlorides of the blood and tissue have fallen to about half their normal level

The chloride recovered from the vomitus and from the contents of the obstructed gastro-intestinal tract at autopsy corresponds fairly closely to that lost from the tissues and blood of the entire organism We have verified this in a large number of dogs, cats and human beings

6 Wilkie, D P D Experimental Observations on the Cause of Death in Acute Intestinal Obstruction, *Brit M J* **2** 1064 (Oct 25) 1913

7 Foster, W C, and Hausler, R W Studies of Acute Intestinal Obstruction, *Arch Int Med* **34** 697 (Nov) 1924

8 Gatch, W D, Trussler, H M, and Ayres, K D Causes of Death in Acute Intestinal Obstruction, *Surg Gynec Obst* **46** 332 (March) 1928

9 White, J C Recherches experimentales et cliniques sur le mecanisme de la mort dans l'occlusion intestinale aigue, *Lyon chir* **25** 622 (Sept-Oct) 1928

10 Wangensteen and Chunn proved that all intestinal contents, even after sterilization by Berkefeld filtration, are toxic when injected intravenously This is the case regardless of whether the material is taken from a normal dog, from above or below a simple occlusion or from a closed loop (A Comparison of the Toxicity of Normal and Obstructed Intestinal Content, *Arch Surg* **16** 607 [Feb] 1928)

Gamble and McIver<sup>10</sup> as well as Atchley and Benedict,<sup>11</sup> published similar results.

The second group may be expanded to include all intestinal obstructions accompanied by impaired blood supply whether this impairment is due to strangulation, mesenteric thrombosis, volvulus, intussusception or simple obstruction with distention. This group carries a far more serious prognosis. Kader<sup>12</sup> in 1892 and Murphy and Vincent<sup>13</sup> in 1911 first showed that interference with the intestinal blood supply (particularly on the venous side) is a vital factor governing the severity of symptoms in acute obstruction.

McIver and White<sup>14</sup> found that cats with experimental volvulus of a section of the middle of the small intestine 20 cm long died in about twenty hours whereas with simple division and inversion of the bowel ends at the same level animals survived from three to five days. Since the animals died rapidly vomiting in the group showing "strangulation" was slight or absent. Consequently, the reduction in the chlorides of the blood and tissue was correspondingly small. The only procedure capable of prolonging life, short of resection of the strangulated gut, was the removal of the strangulated gut to the outside of the abdominal wall. This evidently prevented the absorption of toxins and completely altered the pictures. Two animals treated in this way lived three and five days vomited profusely and died when they had lost half the chloride of the body. In other words, an obstruction of the second type was converted into one of the first.

The evidence in favor of death by absorption of toxins in the second group is overwhelming. Practically all experimental and clinical observers are agreed on this. Therefore, the discussion at the present moment concerns the first group. The experimental work reviewed makes a fairly strong case against the importance of toxemia when the mucosa has its normal blood supply. If a potent toxin is being absorbed, it is difficult to see how salt solution could sustain life in these cases, since it has no appreciable effect in combating the toxemia in the "strangulation" group.

It occurred to us that the toxemia theory in the simple high obstructions would be rendered even more untenable if an animal with such

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11 Atchley, D W., and Benedict, E M. The Distribution of Electrolytes in Intestinal Obstruction. *J Biol Chem* **75** 697 (Dec.) 1927.

12 Kader, B. Ein experimenteller Beitrag zur Frage des localen Meteorismus bei Darmocclusion. *Deutsche Ztschr. f. Chir.* **33** 214 1892.

13 Murphy, F T. and Vincent, B. An Experimental Study of the Cause of Death in Acute Intestinal Obstruction. *Boston M. & S. J.* **165** 684 (Nov. 2) 1911.

14 McIver, M A. and White, J C. The Role of the Bacillus Welchii in Acute Intestinal Obstruction. *Ann Surg.* **89** 647 (May) 1929.

a condition could be kept alive over a considerable period simply by restoring the materials lost in the vomitus through an ileostomy below the point of obstruction. In such an event, it would be illogical to believe that the obstructed contents contain any important absorbable toxin. Furthermore, if no additional salt were given, it also would be impossible to claim that toxins in the tissues are neutralized by an excess of chloride ion.

#### EXPERIMENT

*Technic*—In order to test this, we operated on a police-dog bitch weighing 140 kilograms, under ether anesthesia, and severed the small intestine 12 inches (30.48 cm) below the pylorus. The two ends were invaginated and buried separately in the omentum. A no. 20 soft rubber catheter was then inserted obliquely (by the Witzel method) into the distal small intestine. The catheter was brought out through the omentum, then through a separate stab wound in the left rectus muscle, and firmly secured by a broad bandage of adhesive tape. The perineum was split toward the rectum, so that the urethral orifice could be seen and the bladder catheterized.

The animal made an excellent operative recovery. It was kept in a cage for use in the study of metabolism, so that the vomitus could be collected, and the animal was catheterized twice daily to prevent contamination of the vomitus with urine. Later, the dog learned to void while outside the cage on a leash. Formed stools were caught on a wire grating, so that fecal contamination occurred only when the dog developed a watery diarrhea. It was given all the water that it would drink.

Three or four times each day all the vomitus, diluted to 200 cc with water, was injected through the catheter into the lower unobstructed small intestine. After three days, we added as much dextrose as the intestine would tolerate, as we wished to prevent a ketosis and to maintain the animal's nutrition as well as possible on a completely salt-free diet. Dextrose, of course, had no effect on the process in question, as Haden and Orr<sup>4</sup> have shown that it does not prolong life in intestinal obstruction.

We were unable to keep up the animal's caloric requirements by dextrose without producing a troublesome watery diarrhea, therefore, it slowly but steadily lost weight. After two weeks, we tried adding small amounts of "Casec," which is a proprietary infant food and is nearly all protein with less than 1 per cent of ash. This was not completely digested, presumably on account of the lack of protein-splitting ferments in the lower bowel.

*Observations*—Table 1 gives the complete record of the dog's intake and output and also its condition from day to day.

In spite of the total high obstruction, the dog remained in surprisingly good condition for the entire month. During this period it remained bright and active, playing with other dogs in the laboratory and jumping in and out of the cage (which was 2½ feet [30 cm] from the floor) through the first fortnight. During the second two weeks, the partial starvation weakened the dog somewhat. The weight sank slowly, but progressively from 14 to 10 Kg. Nevertheless, the animal remained as bright and alert as at the beginning of the experiment.

The chemical changes in the blood and tissues are shown in table 2. There was essentially no change in the plasma bicarbonate and non-protein nitrogen throughout the entire month. The chloride fell slowly to 410 mg. in the blood plasma and to correspondingly low levels in

TABLE 1—Data on Metabolism

Days After Operation	Output			Intake				Weight Kg.	Comments
	Vomitus Cc.	Urine Cc.	Stool Cc.	Nacl Cc.	Nacl Cc.	Mouth Cc.	Rectum Cc.		
1		700				500	550	11 00	Good operative recovery
2	Trace	900		Trace			400		
3	700	700		21+	21	200	700		Dog in good condition
4	500	750	70	20+	20	1 000	750	13 80	
5	580	220	500	24+	24	1 000	750		From this point on 75 Gm of dextrose (average dose) was injected daily through ileostomy
6	1 430	325	500	71—	52	1 000	1 400		
7	170	1 130		07+	07	1 000	1 200	13 10	Dog active
8	900	900	620	35—	35	1 000	1 000		
9	190	680		Trace		1 000	1 190	12 50	
10	300	940	Trace			1 000	950		Slightly lethargic
11	600	580		34+	34	500	850		
12		400	400			1 000	900	12 20	Bright and active again
13		240	750			1 000	1 200		
14	345	120		11—		500	900	12 00	A little weak as she lies down when left alone
15	250	442 (mixed)		12+	12	500	1 200		
16		1 250 (mixed)					900	11 80	
17		1 320 (mixed)				500	1 200		
18		810 (mixed)					1 200	11 50	During second half of experiment 25 Gm of Casec (average) was injected daily through ileostomy
19		1 380 (mixed)				500	1 150		
20		1 000 (mixed)					950	11 45	
21		600 Trace				680	1 270		Again active
22		1 000 (mixed)				1 000	1 200		Dog beginning to weaken and fairly emaciated mentally bright and interested in surroundings
23	260	500	100	15+	15	500	950		
24	20	400	100	Trace	Trace	500	1 200	10 60	
25	100	500	200	06+	06	500	1 200		
26		1 480 (mixed)					1 150		Dog lies down but walks about when taken out of cage
27		820				260	900		
28		825						10 00	Dog killed autopsy

TABLE 2—Chemical Data

Days After Operation	Tissues		Blood		CO per Cent
	Skin Cl Mg	Muscle Cl Mg	Chloride Mg	Nonprotein Nitrogen Mg	
Before operation	380*	190*	650*	30*	56.0*
3			599	33	
9			535		
11			474	24	52.2
18			440		57.6
21					56.0
28	215	101	410	33	63.2

\* Preoperative figures are based on average normal values. Chlorides are expressed as milligrams of sodium chloride per hundred grams of tissue or plasma, nonprotein nitrogen in milligrams per hundred cubic centimeters of plasma, and carbon dioxide in volumes percent of the plasma.

the muscles and skin. In untreated dogs, vomiting as much as this one did, a similar reduction would have taken place in from three to five days. The slow loss of chloride, which for the month amounted to about 40 per cent, can be accounted for in the small daily loss of vomitus



Postmortem specimen showing stomach with dilated obstructed duodenum above, *a*, obstructed upper segment showing complete occlusion by inversion of the jejunum. Below distal unobstructed segment of the upper ileum with catheter inserted obliquely through the skin and abdominal wall. *b* indicates the inverted proximal end of the lower collapsed segment, *c*, the catheter enterostomy.

and in the diarrheal stools. When these were mixed with vomitus they were reinjected through the ileostomy, but when recovered pure or mixed with urine they were rejected. No appreciable elimination

occurred through the urine after the third day (it is well known that as the blood chloride level falls the kidneys stop secreting salt)

At the end of a month, the dog although somewhat weak from the prolonged low intake of food (it received on the average 250 calories a day which amounted to only 50 per cent of the calculated maintenance diet), appeared to be in good health and did not give the impression of being dehydrated or extremely emaciated. But as we did not wish to subject the animal to unnecessary suffering and felt that a month was sufficient to demonstrate that life could be maintained by restoring the substances lost in the vomitus it was killed by the administration of ether on the twenty-eighth day of the obstruction. Autopsy showed that the obstruction had remained complete and revealed no other gross abnormalities (fig.)

#### COMMENT

By this experiment we have demonstrated that an animal with a total obstruction of the upper small intestine can be kept alive and in good health as long as the loss of digestive secretions is prevented and the nutrition maintained. We are not urging this as a therapeutic panacea, since both animals and human beings with this type of obstruction do so well with injections of physiologic solution of sodium chloride. Whether the biliary, pancreatic and gastroduodenal secretions contain other substances vital to life besides sodium chloride is beyond the scope of this paper. But this animal remained in much better condition with the restoration of its own vomitus and lived much longer than any which we treated with injections of salt and dextrose.

The point we wish to bring out is the absence of toxemia in this type of obstruction. The presence of absorbable toxic substances in the dammed-up gastro-intestinal contents is inconceivable when it was through their injection that life was preserved. It is equally inconsistent to claim that hypothetical toxins in the body can be neutralized by the chloride radical, when no extraneous salt was given and its content in both the blood and the tissues was considerably reduced during the experiment.

In our experimental animals and in a large number of patients with this type of obstruction who have been studied in the Massachusetts General Hospital the same generalized dechlorination—tissues  $\text{Cl}$ , blood  $\text{Cl}$ , vomitus—invariably has occurred. Tables 1 and 2 show that this process has taken place slowly here. With it there has been no corresponding rise of nonprotein nitrogen or increase in the excretion of nitrogen by the kidneys which one would expect if a proteolytic toxin were being absorbed. To reinforce our argument from another angle it may be pointed out that in the group showing 'strangulation' in which toxemia is profound there often is a normal chloride level in the blood and injections of salt solution are not of the slightest use.

in preventing the rise in nonprotein nitrogen or in combating the toxemia<sup>15</sup>

Experimental evidence in the papers cited points strongly to dehydration as the cause of the nitrogen retention in the simple high obstructions. It is most surprising that this animal did not become dehydrated, as during the course of the month we were unable to prevent a considerable loss of blood base, as well as chloride. (The blood base fell from a normal of 160 cc of 0.1 normal base per hundred cubic centimeters of serum to 131 cc.) It is beyond the scope of this paper to go into the physiology of the acid-base equilibrium and its application to this case, but it is probable, on account of the gradual depletion of sodium and chloride, that the organism was able to compensate for the loss of electrolyte and to maintain the water content of its tissues in some unknown way.

In this connection, it is interesting to note that the dog was able to absorb as much as a liter (1,000 cc) of water a day through the upper 12 inches (30.48 cm) of the small intestine. After the first week of the experiment, the dog began to adjust itself to the new conditions by vomiting less and less. Thus, during the first week, it vomited 3,180 cc, during the second, 2,335 cc, during the third, 250 cc, and during the fourth 380 cc.

Since this experiment was performed, we have read the paper of Raine and Perry<sup>16</sup>. They showed that when a rabbit is given a simple jejunal obstruction, death follows in from twenty to thirty hours. As the rabbit is unable to vomit, all the obstructed secretion remains in the dilated stomach and duodenum. When the obstruction is released just before the animal is moribund, the obstructed secretions pass down the intestine and are absorbed, and the animal's condition rapidly improves. The removal of the stomach contents and their replacement by distilled water, before the obstruction is removed, greatly retards recovery. This experiment showed in another way that no potent toxin is absorbed in simple high obstruction, and that it is the loss of the digestive secretions that causes death.

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15 It must not be forgotten, however, that most cases of human intestinal obstruction are mixtures of the two types, a volvulus or an intussusception occludes the lumen of the intestine, as well as shuts off its blood supply. Therefore, if these patients live long enough, they usually vomit and dechlorinate to a certain extent. They may even secrete a considerable quantity of chloride into the obstructed gastro-intestinal tract without vomiting. For this reason, in every case of intestinal obstruction salt solution should be used, although its effect in the second group is slight in comparison with that in the first.

16 Raine, F., and Perry, M. C. Intestinal Obstruction. Experimental Studies on Toxicity, Intra-Intestinal Pressure and Chloride Therapy, *Arch Surg* 19: 478 (Sept.) 1929.

## CONCLUSIONS

1 A dog with a complete high intestinal obstruction was kept alive and in good condition for a month. This was accomplished by preventing the loss of its digestive secretions, these being immediately reinjected into the lower unobstructed bowel.

2 It is extremely unlikely that any potent toxin formed in the obstructed intestine can be absorbed by the mucous membrane as long as its blood supply is maintained. Otherwise, life would have been shortened rather than prolonged by the reinjection of the obstructed secretions.

3 The theory that the beneficial effect of salt solution is due to the neutralization of toxin by the chloride radical seems illogical. This animal received no salt from outside sources and became considerably dechlorinated during the prolonged obstruction, owing to a small unavoidable daily loss. The dechlorination of the tissues corresponded to that of the blood.

4 As the nonprotein nitrogen and nitrogen output in the urine remained normal there is no evidence that tissue protein was destroyed by toxin.

5 We believe that death in the uncomplicated high obstructions is due mainly to loss of salt and water, possibly also to other substances, in the gastroduodenal secretions. When inorganic electrolytes are lost rapidly and are not replaced, it becomes impossible for the organism to retain its normal water content. This leads to fatal changes in the physiochemical equilibrium of the blood and tissues.

NOTE—While this article was in press, Dr W. H. Snyder and one of us (J. C. W.) repeated these observations on a second dog. This animal was given a complete obstruction at the same level and was observed over a period of two weeks. During this time the dog received only its vomited digestive secretions plus water and dextrose, which we injected through an enterostomy in the upper end of the distal small intestine. The animal reacted in every way like the one in the experiment reported, remaining in excellent condition except for a similar slow fall in blood chloride and body weight. There was again no evidence of toxemia or dehydration. The absence of dehydration was noticed clinically in the first dog, but in the second it was confirmed by laboratory tests as well. There was no increase in the plasma protein nor any appreciable change in the erythrocyte count or the hematocrit reading.



# TUMORS OF THE ORBIT

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NEW ORLEANS

In this paper I report four types of tumor of the orbit with which I have had personal experience (1) osteoma of the orbit, (2) epithelioma of the lids and of the bridge of the nose, (3) carcinoma of the lacrimal gland and (4) melanoma

In some of these cases exenteration was required, and in one all the manifestations were relieved by removal of the primary growth

They are included in a single report because of the following facts All the growths involved either the walls of the orbit or its contents In some instances the growths involved the orbital contents other than the globe This happened in the malignant cases which began primarily as epitheliomas of the lid and the bridge of the nose or as carcinoma of the maxillary antrum In these cases the growths began outside the orbit and later involved its contents

In some instances there were manifestations of disturbance of vision from encroachment on the orbital contents and consequent displacement of the eye itself In some instances exenteration was necessary in spite of the fact that there was no invasion of the globe, and because radical removal of the growth would have left the eye without proper protective covering

In one of the cases which excited a great deal of interest, the growth seemed to have originated within the globe, either as a melanoma or as a glioma of the retina It destroyed the eye so completely that in the gross specimen it was difficult to identify the various structures of the eye

There were two osteomas of the orbit, on only one of which I operated This I believe to have been a fronto-orbital osteoma

## OSTEOMA OF THE ORBIT

The two cases cited represent the only bony tumors of the orbit I have had occasion to see The apparent rarity of the condition excited my interest, and after a search of the literature it seemed worth while to report them because so far as I can find there are not more than 250 cases recorded

It will not be necessary to review the literature extensively The first case was recorded by Veigas in 1506 (Bedell) Andrews, in 1887,

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\* Submitted for publication Dec 21 1929

collected reports of all the cases that he could find up to that time. He reported sixty which had been already recorded and forty-eight for which he found records among 429,989 cases of disease of the eye which had been observed in the New York Hospital from 1821 to 1887.

William F. Smith reviewed the literature again in 1888. In 1904 Le Grange found 148 cases. Culbert in 1918 found records of 215 cases from 1748 to 1918.

The subject of orbito-ethmoidal osteomas (a selected group from within the larger group) was considered by Dr. Cushing of sufficient importance to be made the subject of his presidential address before the American Surgical Association. In this address he recorded four cases which had come under his observation. Cushing stated that Dr. A. S. McWilliam of the Massachusetts Eye and Ear Infirmary had seen only one of these lesions after an experience of 15,000 examinations of roentgenograms of sinuses.

In reviewing the cases which have been reported one finds confusion particularly with reference to the origin of these tumors. It would seem worth while to classify all bone tumors found within the orbit as orbital osteomas and under this general heading to have subdivisions that would indicate their point of origin and the etiology.

Cumston in 1920 gave a definition that should satisfactorily meet this demand. He said: "Osteomata of the orbit are bony growths which reproduce all varieties of bone tissue taking their origin in the walls of the orbit itself or in the neighboring cavities, such as the ethmoidal cells, nasal fossae, antrum of Highmore and more frequently of all the frontal sinus." This definition permits the inclusion of exostoses in the term osteomas.

Virchow, discussing the origin of these tumors, stated:

Although there is scarcely any part of the orbit where these bone tumors have not been found the upper and inner part however, are by far the most frequent sites. It is understandable how difficult it may be to determine whether a tumor has originated primarily in the nasal or frontal sinuses or in the orbital cavity, whether it comes from the inner or outer surface of the bone, finally whether it originated from the frontal or ethmoid bone or somewhere else. For all these possibilities there is evidence in the literature without it being always possible to determine the correctness of either opinion. For a tumor which arises from the interior of the frontal bone can very well later on project into the frontal, orbital, nasal or cranial cavity.

Cushing in 1927 was prompted to say:

Whence may well be asked does the original tumor arise and what is the significance of its apparent relation to a preceding injury? Doubtless mild frontal injuries may more often than suspected produce a fissured fracture of the thin floor of the anterior cranial fossa, it not a fracture of diastasis. It is not inconceivable that some quiescent cartilaginous anlage may have been stimulated to bone productive activity.

Birch-Hirschfeld, in 1906, differentiated between the encapsulated osteoma and an exostosis. The encapsulated osteoma he found had a tendency to grow toward the brain. These tumors arise in accessory nasal cavities and then extend into the orbit. In the exostoses there is a history of trauma, and they usually arise from the upper inner orbital walls and grow out into the orbit.

William F. Smith as early as 1888 said

There are three points or characteristics which should distinguish osteomata from exostoses. They are (1) the origin of the tumor from one of the bony cavities, (2) the encapsulating membrane, and (3) the ivory hardness. The osteoma rarely, if ever, has a traumatic origin, the exostoses nearly always have a history of trauma and are developed from the periosteum.

#### GENERAL OBSERVATIONS

*Age*—Bony tumors within the orbit are found largely among young people. According to Culbert, 50 per cent occur during adolescence and 30 per cent more before the patients reach the age of 30.

*Location*—The tumors may be located at any point within the orbit, but the most common site is the upper inner wall. They may take their origin from the frontal bone, the frontal sinus, the ethmoid bone or from periosteomas.

According to Gerber, "the proportion of tumors arising within the ethmoid is as 12 to 8 to those arising in the frontal sinus." In osteomas of the frontal sinus the largest proportion of the growth is in the sinus and only a small part, according to Lebensohn, projects into the orbit.

Osteomas of the frontal sinus perforate the walls of the sinus and enter the orbital cavity, they may perforate into the cranial cavity. The latter is a point of great importance and one which has been particularly emphasized by Cushing as an indication for a cranial approach rather than an intra-orbital approach.

*Period of Development*—Osteomas are slow growing. In many instances several years elapse before they produce sufficient annoyance to cause the patient to seek relief.

The size of these growths varies. In the earlier literature, there are records of cases in which the growths attained "the size of a child's head." In one instance, the tumor measured "7½ inches in circumference and 2¾ inches in thickness."

#### DIAGNOSIS

Prior to the use of the roentgen ray, the diagnosis could be made certain only at operation. Because of the great service which the roentgen ray renders cases that could not otherwise be diagnosed are now found, and in some instances these growths have been found in the

course of an examination of the sinuses when no suspicion of their existence had been aroused in the mind of the surgeon.

There are few outspoken manifestations. However a number of signs and symptoms have been found sometimes in association and sometimes independently. Little pain is associated with some of them. There may be severe headache which is usually intermittent rather than continuous.

Cumston stated that there may be a neuralgic pain which is transmitted along the fifth cranial nerve. Diplopia is sometimes present but has not been a constant manifestation. The globe may be dislocated in varying degrees. Exophthalmos of varying degrees is the most constant manifestation. If dislocation takes place it is very slow and, according to Gerber, the direction of the dislocation gives an idea of the location of the tumor. He says, "When the protrusion is exceedingly outwards a tumor of the ethmoid is inferred, where the globe is directed upwards the maxillary sinus is involved while a propulsion forwards, outwards and downwards is pathognomonic for tumors of the frontal sinus."

A visual disturbance, according to Cumston, is often related to the exophthalmos. He further says that the "displacement of the eye is necessarily accompanied by traction on the nerve, which, combined with the pressure exercised by the growth, brings about changes in the fundus usually phenomena of stasis, a more or less marked coloring of the papilla due to engorgement of the veins, arterial anemia or even ischemia resulting from compression or the return circulation."

In this connection it is interesting to note that in spite of the indolent nature of the growth it has been said that removal of the tumor sometimes results in considerable improvement of vision.

Negative evidence is sometimes as valuable as positive evidence. There is one negative observation that has aroused the interest of observers, particularly that of Cushing, who called attention to the absence of rhinologic symptoms in spite of the association of these growths with the paranasal sinuses.

It will be noted by reference to case 1 here reported that there was no evidence of disturbance of the various sinuses.

#### PROGNOSIS

These growths are histologically benign, but because of the effect produced by pressure, Lebensohn has properly remarked that they are clinically malignant. When one considers the complications in patients who are not operated on, such as exophthalmos, optic neuritis, optic atrophy, sinus infection perforation of the roof of the orbit into the cranium with a tendency to cerebral compression one can readily under-

stand the danger of allowing these growths to remain in an unoperated condition

According to Birch-Hirschfeld's statement in 1907, the mortality is as follows in those originating in the "frontal sinus without operation 48.2 per cent, after operation 13.6 per cent, ethmoid 80.0 per cent without operation, after operation 12.7 per cent, sphenoid without operation 100.0 per cent, after operation 33.0 per cent." No further plea need be made for operation.

The method of approach most commonly used has been through the orbit by an incision such as is described in this paper. Cushing advocates a cranial approach in orbito-ethmoidal osteomas. He considers either a nasal or an orbital route "awkward" because "neither method of approach makes allowance for the possibility that the tumor may have extended into the intracranial chamber."

#### REPORT OF CASES OF OSTEOMA OF THE ORBIT

CASE 1—L. R., a man, aged 35, with intra-orbital osteoma, was referred for consultation by Dr. A. R. Crebbin, an ophthalmologist. The following is a brief summary of the history as taken from the record.

The patient was admitted to the Touro Infirmary on Sept. 11, 1928, complaining of pain over the eye. The left eye had begun to swell five years before. The swelling remained for three days and then subsided. The patient had had no further trouble until two weeks before. During the past five years he had had frequent headaches, the pain being greatest over the left eye. At times nausea had been associated with the headaches. There was no history of nasal trouble, and the sight had been good. Dr. Crebbin reported no pertinent symptoms of the eyes, vision in both eyes was normal and the fundi were normal. The Wassermann reaction was negative.

Prior to the time that I saw the patient, a roentgenogram had been taken of the skull. Dr. Henderson reported the presence of a large osteoma occupying the area from the superior boundary of the maxillary sinus up to and involving the frontal plate of the skull over the frontal sinus. This likewise extended as far backward as almost to come in contact with the anterior boundary of the sphenoid, thus occupying the major portion of that area normally occupied by ethmoid cells. The point of attachment and origin could not be definitely determined. However, its densest portion was its lowest segment and as it approached the frontal sinus and sphenoid, it could be seen to thin down. This was a fairly large osteoma which had many points of contact with and origin from the surrounding structures.

On September 14, I was called to see the patient and noted the following conditions:

The axis of the left eye as well as the palpebral fissure was almost 30 degrees above the horizontal axis of the right. There was fullness at the inner canthus of the left eye. No prominent bony masses were noted over the maxilla. There was a hard bony prominence which impinged on the orbit at the inner canthus of the left eye.

Dr. Weil was requested to examine the nose and throat. He reported moderate deflection of the septum to the right but sufficient breathing space. The nose was

between the nasal process and the upper margin of the orbital rim and the orbital contents were held in place by the teeth.

After considerable study Dr. Wells reported and the roentgenogram was decided to approach the tumor from directly through the orbit displacing the orbital contents.

An incision was made along the supra-orbital ridge and the inner side of the nasal bone medial to the inner canthus and then prolonged obliquely downward and parallel to the infra-orbital ridge. The original incision was carried down to the bone. Bleeding was controlled by pressure and clamp.

The periosteum was reflected and retractors were introduced into the orbit so as to retract the orbital contents. When this was done a large bony mass was seen closely approximated to the nasal and lacrimal bones, the greater portion of



Fig 1 (case 1)—Appearance of orbital osteoma before operation

it was free occupying the nasal third of the orbit. The mass had a number of "bosses" on its surface. It seemed to lie under the overhanging edge of the nasal and lacrimal bones. The inner aspect of it and the lower surface were not adherent to the nasal side of the orbit. The only point of fixation was its attachment, the frontal bone. With the chisel the overhanging portion of the nasal and lacrimal bones with the inner margin of the infra-orbital ridge, or nasal portion of the maxilla, were chiseled away. The chisel was used partially to detach it from the nasal portion of the frontal bone. A grooved director could then be inserted between the perpendicular plate of the ethmoid and the growth as well as at the base of the orbit.

With a pair of bone holding forceps the growth was grasped. It may be noted here that the forceps had to be taken apart and applied very much as obstetric forceps are applied. After the forceps were on it was possible to remove the growth without injuring the eye or any of the contents of the orbit. There

was no active bleeding. A pack was introduced for a few seconds until the field was clear. When the pack was removed, it was seen that the growth had not invaded other structures.

There was apparently no communication between the nose and the orbit. There was no opening into the antrum. The impression that I gained at this time was that the growth had increased the size of the orbit and had not invaded the ethmoid, but had rather displaced the perpendicular plate of the ethmoid to the nasal side, thus compressing or obliterating the ethmoid sinus.

A gauze pack was introduced into the cavity and petrolatum strips were applied over the eye. Before putting the bandage on, I noted that there was no conjunctival or subconjunctival hemorrhage. The two pupils were of the same size.



Fig 2 (case 1)—Appearance of skull after operative removal of the orbital osteoma.

The postoperative diagnosis was intra-orbital osteoma.

Following the operation, there was no disturbance of the eye. The patient left the hospital on September 30, eleven days after the operation.

Before he was discharged, however, a roentgenogram was taken, on which Dr. Henderson reported as follows: The area in which a large osteoma had been previously observed was clear, the ethmoid cells had been destroyed on this side but their walls near the outer margins were intact. Apparently all of the tumor had been removed, and the residual structures were considered to be normal.

On Dec 1, 1929, the patient had perfect movement of the eye. There had been no evidence of an epiphora and no disturbance that would indicate injury to the orbital contents.

This case is of interest for many reasons. 1 The only tumor produced by the tumor was pain over the eye and repeated headache. 2 At no time did the patient complain of diplopia. 3 Examination

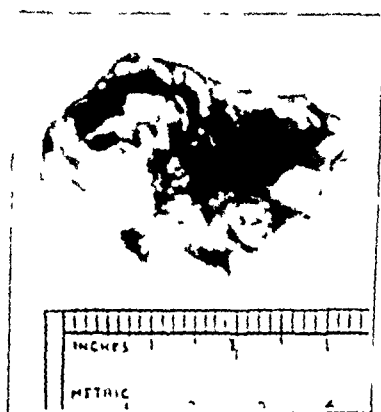


Fig. 3 (case 1) —Osteoma removed from orbit



Fig. 4 (case 1) —Appearance of patient more than a year after the removal of the orbital osteoma

revealed the absence of exophthalmos and the only distortion was a change in the axis of the eye. 4 There was no history of trauma and yet the growth did not seem to have its origin in any of the sinuses the



only attachment being to the under surface of the frontal bone 5 The entire tumor was within the orbit and not within any of the sinuses This last fact is of importance because the majority of so-called exostoses have been associated with a history of an injury and the osteomas which have sprung from the various sinuses are found to extend from the sinus into the orbit 6 When one considers the great size of this bony tumor surprise must be felt that it did not cause some disturbance of vision, particularly diplopia 7 The approach through the orbit and



Fig 5 (case 2)—Orbital osteoma probably springing from the wing of the sphenoid in a boy aged 13

the displacement of its contents laterally permitted a comparatively easy removal of the entire growth 8 The cavity from which the growth was removed was packed because it was feared that possibly an infection of the orbit might take place from the nose, as it was not unlikely that some of the ethmoid cells might have been opened

Since the operation the patient has had no limitation of motion of the eye in any direction, indicating that there had been no disturbance of the muscles within the orbit

A second case of orbital osteoma springing from the wing of the sphenoid has been observed The location of the tumor has not been

1. *Introduction*

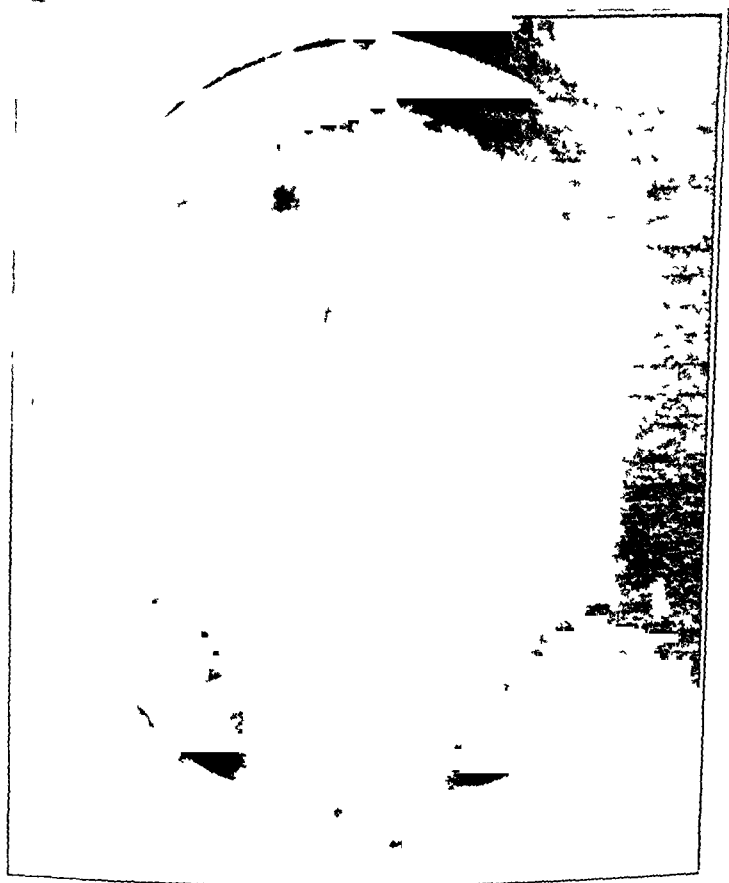
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Fig 6 (case 2) —Orbital osteoma

one-third to one-half inch more than the right. There was a more or less irregular conical cornea with degenerative changes in the upper third of the cornea. The entire eye was enlarged and protruded (buphthalmos) though the corneal dimensions themselves showed little or no increase. The lower lid did not show any abnormality but the upper lid was retracted back into the orbit by some type of adhesion at the junction of the outer quarter with the inner three quarters. Below this was a mass covered with conjunctiva about the size of a white bean which was somewhat compressed and moved somewhat as the eye or lower lid moved. The conjunctiva over this was red and brawny as was the conjunctiva in the upper portion of the eyeball. This was from exposure to the air caused by the fixed

upper lid. The anterior chamber was fairly deep as a result of the conical shape of the cornea. The pupil was centrally placed and reacted well in accommodation to light. So far no view of the fundus had been obtained.

On April 17, 1928, a roentgenogram was taken, on which Dr. Henderson reported as follows: On the left side there was a dense clouding of the osseous tissue which did not, however, involve the antrum on that side, the walls of a somewhat nodular tumor were very well outlined involving the orbit. The structural changes seen were considered to have been produced by a benign tumor of the osteoma type, rather than a malignant growth.

Dr. Weil found no evidence of involvement of the sinuses.

On examination, April 19, I observed a mild proptosis of the left eye, with recession of the upper lid, particularly the outer half, and a bulging of the palpebral conjunctiva. Examination of the rest of the eye had already been made. Retraction of the mandible was apparently greater on the left than on the right side. There was no evidence of facial paralysis. The lower central incisors were at least half an inch posterior to the upper incisors. The patient was able to separate his teeth, which were markedly irregular. The soft tissue about both cheeks was not infiltrated. There was no pain or fulness over either zygoma or temporal fossa. When the patient opened his mouth, contraction of the depressors of the jaw could be seen. There was no apparent movement of the temporomandibular articulation. The diagnosis was ankylosis of the left temporomandibular articulation and osteoma of the orbit.

Roentgenograms of both temporomandibular joints were suggested to determine whether the ankylosis was unilateral or bilateral. Operation was advised.

On April 19, a roentgenogram was taken. On the right side the temporomandibular articulation was identifiable, although there was some atrophy in the ramus of the mandible. On the left side the temporomandibular articulation was completely wiped out and there appeared to be a well defined union.

From the clinical examination and the roentgen observations it was concluded that the child had an intra-orbital osteoma and an ankylosis of the temporomandibular articulation.

The parents refused to consent to operative removal of the osteoma. They were anxious to have plastic operations on the lids for the protection of the cornea. These operations were done, but as they are not pertinent to the subject no further reference will be made to them.

#### EPITHELIOMA OF THE LID (SQUAMOUS CELL TYPE)

The cases of epithelioma of the lid under discussion are those which required eventual evisceration.

There is no need to review the literature, as this has been done many times. A particularly valuable review can be found in the "American Encyclopedia of Ophthalmology."

All forms of treatment have been used and advised in the handling of these cases. Those patients whom I have observed had had a lesion for a long time. All had been subjected to various forms of treatment, including irradiation with the roentgen ray and radium.

Certain observations have been made in all my cases, and my experience does not seem to differ from that recorded in the literature. These growths are slow in development and recur frequently, and unless

radical procedures are adopted they extend into the orbit without affecting the globe. Metastasis to the glands of the neck is a late manifestation. They may and often do erode the bony parts of the orbit, particularly the supra-orbital plate. When this occurs the frontal lobe may be seen in the orbit. Late metastasis to the brain occurs. At times there is erosion of the ethmoid and involvement of the ethmoidal sinus.

There is considerable difference of opinion with reference to the best method of treatment for these cases. Desiccation is preferred by Clark and Wexth. In 1914 Clark said: "After excision of epitheliomas of the canthi no matter how thoroughly the work appears to have been done there is a percentage of recurrence. In such cases if excision is practiced a second or third operation results in exposure of the eyeball notwithstanding the best plastic work. This is not true of desiccation." He stated further: *"that operative surgery is efficient if performed radically but the cosmetic results leave much to be desired."* Secondary plastic operations often improve this condition but more often fail. The best argument against operative surgery in the treatment of these lesions is the fact that cases are being continually referred for other treatment by the highest exponents of the art of ophthalmic and general surgery.

I have used surgical excision, with immediate plastic repair, and endothermy or surgical excision without immediate repair. Radium has been used as a routine in the after-care. All measures have been disappointing.

One of the cases (case 5) may be cited to illustrate the method of treatment and the end-results. The patient, a man, aged 65, first came under observation in 1923. He was subjected to several operations over a period of four years in an effort to effect cure without exenteration.

This case presented an opportunity to watch the results of wide excision and plastic surgery, both of which were of no avail. A recurrence finally necessitated exenteration.

It might be well to digress a little to discuss this experience in detail. The growth involved the major portion of the lower lid, the external canthus and a small portion of the upper lid. After wide excision of the growth, the defect to be closed was great. In an attempt at repair it was necessary to observe those fundamental principles of plastic surgery so well outlined by Gillies, Blair Davis and others particularly to replace not only skin but supporting structures, such as the tarsal cartilage, and to avoid the embarrassment of having hair-bearing skin as part of the transplanted skin.

In my effort to replace the lower lid, a pedunculated graft was taken from the temporal region and a piece of cartilage was taken from the ear. In this instance skin was used to replace the palpebral con-

junctiva We used this in spite of the fact that Gillies in his monograph stated that he had used it only when an artificial eye had been implanted The skin did not act as an irritant to the eye

In Buedinger's operation skin is also used to replace the palpebral conjunctiva R E Wright described the operation as follows

Briefly it consists in removal of the lower lid and its conjunctiva by two incisions starting at the canthi and meeting on the cheek below The triangular skin defect thus produced is made good by carrying a horizontal incision from the outer canthus for a distance somewhat parallel to the other side of the triangle The flap thus defined is dissected up with its superior side in the position originally occupied by the free edge of the lower lid Before anchoring it, however, the tarsus and conjunctiva are replaced by a composite flap from the back of the ear This consists of semilunar pieces of skin and cartilage, still attached to each other, and having a common straight edge somewhat shorter than the edge of the cheek flap The skin is approximately three quarters of a circle, the cartilage one quarter This flap is applied to the deep surface of the skin flap from the cheek, straight edge to straight edge, the surface epithelium of the ear skin towards the globe It is held in this position by two or three double-armed sutures which are passed from behind forward a short distance below the free edge, and tied externally on beads The triangular bare area on the cheek is filled in by a graft as soon as possible

Cartilage from the ear forms an ideal replacement for a lost tarsus

This is not the place to discuss the relative value of any two operative procedures, nor is it my desire to do so It can be said, however, for the procedure used in this particular case that the lid formed by the plastic operation served its purpose for a period of about four years In the interim, however, the patient developed recurrences that necessitated operative procedures for the removal of the new growths

In spite of all efforts it was necessary to exenterate the orbit in April, 1927, as the growth had by this time caused so much exposure of the conjunctiva that the patient was showing evidence of infection and ulceration of the cornea

It should be stated that the lid made by the plastic operation, during the time that it remained, was sufficiently under the control of the patient so that the cornea was almost completely covered when he attempted to close the eye

#### GENERAL OBSERVATIONS

Recurrences in epitheliomas of the lid appear in or near the site of the previous lesion in spite of wide excision and plastic surgery These recurrences necessitate operative procedures which eventually expose the conjunctiva and cornea to such an extent that irritation and infection inevitably follow When this happens, there is no alternative, the orbit must be exenterated Enucleation is not sufficient, as the disease often has extended into the tissue about the eye, even though no disturbance

of vision exists. This is especially true if the growth has its origin on the nose near the inner canthus. Extension of the growth into the orbit is the rule in this group.

At times exenteration seems unnecessarily radical because the patient has an eye that is useful yet when the orbit is invaded surgically granulomatous masses are found which in some instances have already invaded the ethmoid antrum and even the cranial cavity.

In the after-care of these cases radium has been used as a routine.

It is surprising how quickly the large defects produced by the exenteration become filled and are covered by apparent normal epithelium. The duration of life after exenteration is surprisingly long in some instances from three to four years.

A brief summary of the three cases of squamous cell epitheliomas in which exenteration was necessary is appended.

#### REPORT OF CASES OF SQUAMOUS CELL EPITHELIOMA

CASE 3—Mrs. L. P. D., aged 60, seen in September, 1921, had first noticed a mole on the nose in 1912. The mass increased in size and extended to the eyelids. Radium was used by the physician in attendance. In September, 1921, an irregular ulcer was found on the bridge of the nose. The lids were edematous. The conjunctiva was injected and a growth extended over the upper portion of the cornea. The preauricular and digastric glands were palpably enlarged. The patient was referred to me by Dr. C. Jeff Miller and Dr. H. N. Blum, an ophthalmologist. An exenteration was done on Sept. 9, 1921, and a radium pack was introduced. The pathologist reported "squamous cell carcinoma."

On April 17, 1922, the patient presented herself again as she had a recurrence. The tumor was excised with a cautery, and radium was applied. During 1922 she had a second recurrence for which a second cauterization was done, followed by high voltage roentgen therapy. Pain was conspicuously absent. The antrum became involved.

The patient survived at least one year longer. She lived about 100 miles from New Orleans and no autopsy could be obtained.

CASE 4—T. M., a man, aged 64, was seen on May 28, 1929, with a diagnosis of epithelioma of the nose and lids, hypertension and arteriosclerosis. About eight months before the patient had noticed a small pimple on his nose which he squeezed. Later an ulcer on the surface was noticed. The growth gradually enlarged. There had been no disturbance of vision. Examination at that time showed an ulcerative area on the bridge of the nose. The growth extended down to the inner canthus. The edges of the ulcer were elevated and there was induration of the surrounding skin. A report from Dr. Weil, otolaryngologist, was to the effect that there was no evidence of a pathologic condition within the nose. A roentgenogram was negative for bone changes in or about the nasal structures.

A preliminary operation was done under local anesthesia. The area to be excised was circumscribed by minute punctures with the diamond-shaped current. The incision resembled a three leaf clover, the middle leaf corresponding to the inter-orbital portion of the forehead and the lateral leaves extending down on the left side to the inner third of the upper and lower lids through their entire thickness and on the right side to the inner canthus. The base line swept over the nose



Fig 7 (case 3) —Section of squamous cell carcinoma removed from the lid

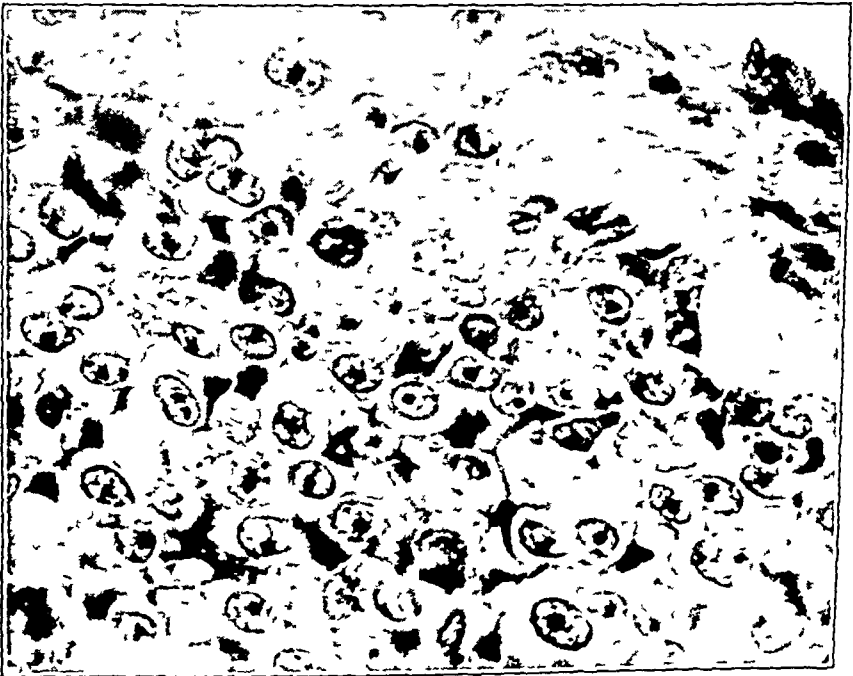


Fig 8 (case 3) —High power view of squamous cell carcinoma

just about half an inch from the tip of the nose at the lower limit of the cartilage. When skin was reflected from the right to the left part of the base of the growth which covered and involved the nasal bone did not come away with the growth.

After entire removal of the flap, care was taken that the nasal bones were covered by a granulosomatous mass and then the question arose whether to attempt to remove the nasal bones entirely and exenterate the orbit. It seemed to me that removal of the nasal bone would leave too much risk of immediate infection, possibly meningitis. I used the current for the purpose of destroying all of the growth that I could see, after which 50 mg. of radium in copper was laid directly on the main portion of the nasal bone. The eyes were protected by a lead screen and 2 inches of gauze.

Following the operation, the radium pack was left in situ. The pathologic diagnosis was squamous cell carcinoma (Linford).

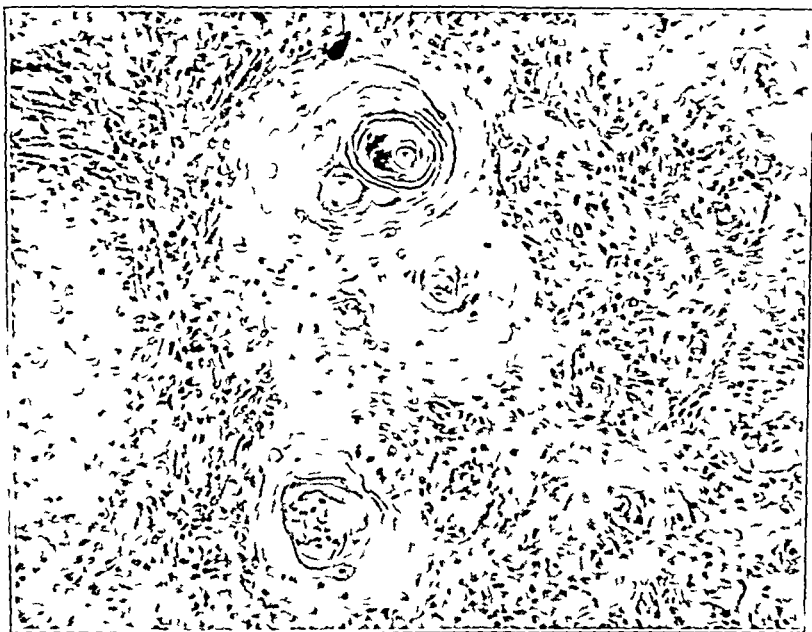


Fig. 9 (case 4)—Low power view of squamous cell carcinoma involving the nose and eyelids.

The patient was discharged from the hospital on June 12. He was readmitted on June 29. At that time a large ulcerated area was observed over the forehead and the root of the nose, extending from about 1 inch above the level of the supra-orbital ridge down to and covering the bridge of the nose. It was about 2 inches long and 1 inch wide. The ulcer involved the inner canthus of the left eye and extended to about one-half inch from the inner canthus of the right eye. It was covered by a grayish exudate. At the junction of the root of the nose and the frontal bone there was an area about three-fourths inch in diameter in which the bony tissue was exposed. The ulcer extended to the border of the left orbit. The conjunctiva of the left eye was pulled down and away from the eyeball by the contraction of the scar tissue. The conjunctiva of this eye appeared red and was inflamed; there was a free flow of tears as a result of irritation of the conjunctiva. About 1 cm. lateral to the margin of the ulcer on the left side there was a small mass situated beneath the conjunctiva. This suggested a distorted caruncle.



Because of the contraction of the scar tissue from the healing ulcer the normal anatomic arrangement was destroyed. The upper lid on the left was edematous and inflamed.

There was a small elevated area on the skin about 1 cm. in diameter situated just to the right of the lower end of the nose. This appeared to be another epithelioma.

Because apparently all of the growth had not been removed, the patient and his family were advised that it would probably be to his best interest to have the orbit exenterated in spite of the fact that it would be necessary in so doing to destroy a useful eye. Accordingly an exenteration was done on July 8. Examination of specimen by the pathologist revealed the fact that the eye itself showed no evidence of neoplasm.

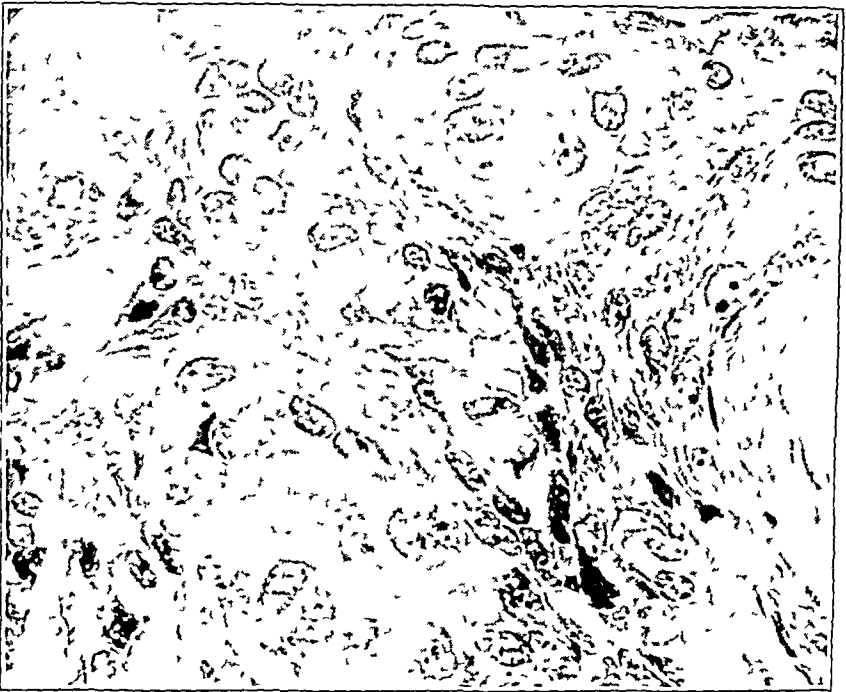


FIG. 10 (case 4).—High power magnification of squamous cell carcinoma.

In these two cases it will be noted that (1) the growth first noticed was a small mass on the nose, (2) the mass later ulcerated and involved the structures of the lid about the inner canthus and in neither case was there any disturbance of vision, (3) at operation the orbital structures, other than the eye itself, were involved, (4) both the patients were conspicuously free from pain.

CASE 5.—A. D., a man, aged 65, first noticed a small growth of the outer canthus five or six years before he came under observation. His chief complaint was that it was causing a deformity of the lower lid. A mass was found on the lower lid at the external canthus. The mass was elevated and consisted of hard ulcer on the surface. The growth had invaded the upper lid at the angle and it involved a greater portion of the lower lid. There was an ectropion deformity of the lower lid and a thickening of the palpebral conjunctiva.

The first operation was done on June 1 1923 under local anesthesia. It consisted in excision of a portion of the upper lid and the entire lower lid. A pedunculated flap was taken from the temporal region and a small piece of cartilage was taken from the helix of the ear. This was implanted in that portion of the graft which was to be used to replace the lower lid. A tubular graft was made out of the major portion of it and the palpebral conjunctiva was thus replaced by skin. The tarsal cartilage was replaced by cartilage from the ear.

The pathologic diagnosis was squamous cell carcinoma.

A number of subsequent operations had to be done in order to complete the plastic repair of the external canthus and to overcome the ectropion deformity which developed. After a time the patient had sufficient control over the lid to

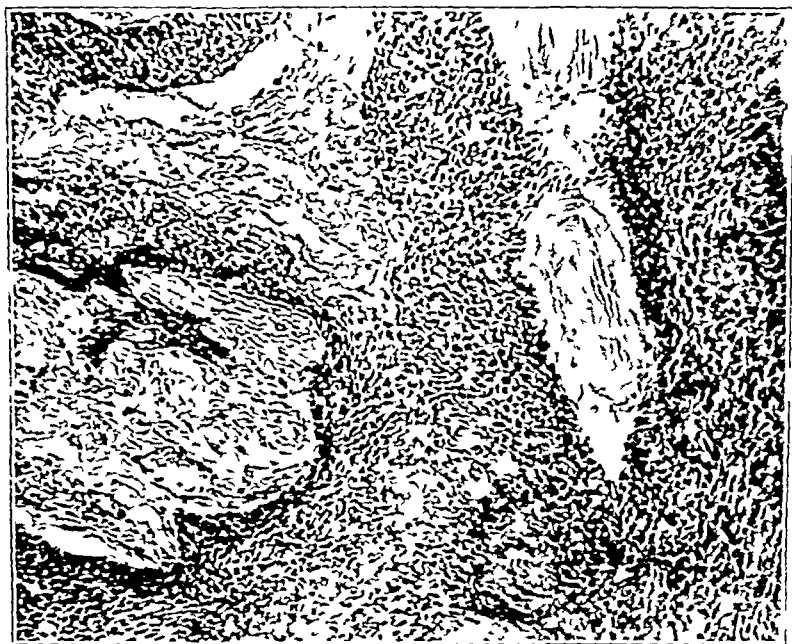


Fig 11 (case 5)—Low power view of squamous cell carcinoma removed from the lower lid and part of the upper lid.

cover the eyeball almost completely when he attempted to close the eye. Recurrences developed one and one-half years later and from time to time it was necessary to excise recurring growths, until finally four years later it was necessary to do an exenteration.

During the whole time the patient's general condition remained excellent and he did not complain of pain. Glands in the digastric triangle did not become involved. The patient survived the operation by more than one year. The cause of death assigned was chronic myocarditis and chronic nephritis.

1 Squamous cell carcinomas of the lid may appear at any portion of the lids. 2 They are slow growing tumors. 3 They recur frequently, metastasize slowly and eventually invade the orbit. 4 After

surgical excision, plastic surgery may save the eye for several years 5 Eventual exenteration is as a rule necessary because of recurrences 6 Whether radium, the roentgen ray or endothermy is better than surgery, alone or in combination, probably is hard to determine because the more radical the measure, the better will be the end-results 7 Disturbance of vision is the exception, resulting in my experience only after there had been an exposure of the cornea 8 Surgical intervention alone or surgical measures combined with endothermy, high voltage roentgen therapy or radium has not resulted in a permanent cure in a single case in my experience Early treatment should give better results

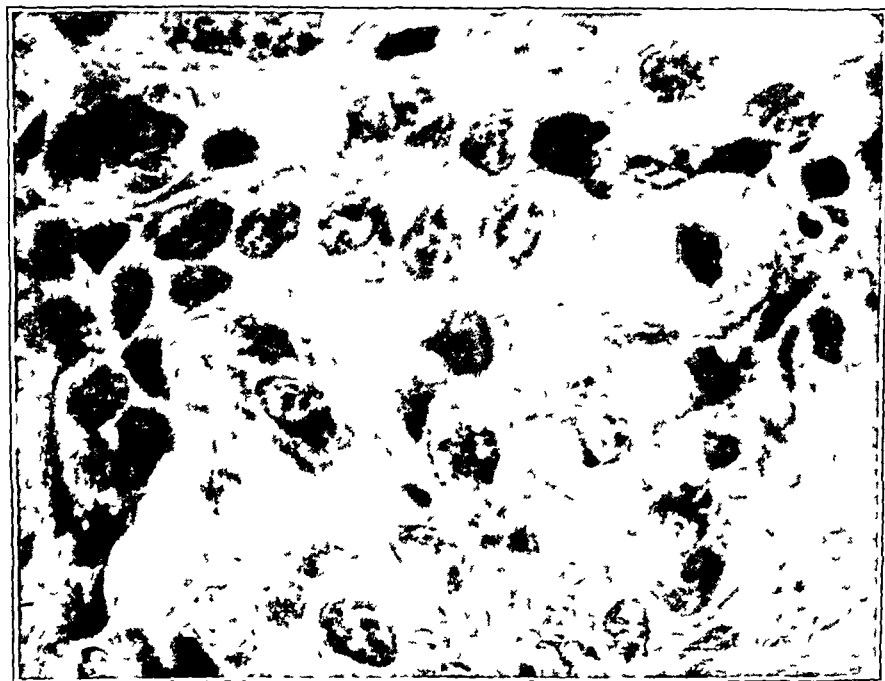


Fig 12 (case 5)—High power magnification of squamous cell carcinoma

#### CARCINOMA OF THE LACRIMAL GLAND

One of my cases belongs in this group The clinical observations may be summarized as follows

CASE 6—Mrs B, aged 45, complained of pain in the orbit of three years' duration The severity of the pain was progressive, there was loss of vision progressive exophthalmos and ptosis At no time could an ulcerating lesion be found The sinuses were normal The Wassermann reactions of the blood and spinal fluid were negative Several doses of arsphenamine did not benefit the patient, and she was referred for operation by Dr H N Blum

Exenteration revealed the fact that the globe was not affected, but there was a large soft mass above and posterior to the eye The supra-orbital plate had been eroded by the growth The frontal lobe could be seen in the orbit

Radium and a pack were introduced into the cavity

The pathologist returned a report of epithelioma from a section examined immediately, and later stated that the tumor was a carcinoma of the lacrimal gland (figs 13 and 14)

The patient lived nearly four years. During the last few months of her life there was evidence of recurrence, the new growth apparently being located in the brain, as the patient had violent headaches, with projectile vomiting followed by symptoms of meningitis and death.

This history and course are characteristic of carcinoma of the lacrimal gland.

According to the literature, carcinomas of the orbit rarely if ever occur as a primary growth except as an extension from a lacrimal gland. Secondary tumors as illustrated by the previous group may involve the



Fig 13 (case 6)—Section of carcinoma of the lacrimal gland seen in the low power field

orbit in connection with new growths of the conjunctiva or other tissues of the lid. These extend inward and may fill the whole orbit. The prognosis is always grave and the treatment, especially in carcinoma secondary to that of the lacrimal gland, is essentially surgical—exenteration of the orbital contents.

#### MALIGNANT TUMOR OF THE ORBIT ASSOCIATED WITH METASTASES MELANOMA OF THE ORBIT

The case of melanoma of the orbit here reported was striking in its clinical aspect and proved to be of even greater interest from an anatomic and histopathologic standpoint.

CASE 7—A, a man, aged 73, admitted on June 11, 1928, to the service of Dr Blum, ophthalmologist, was referred for consultation with the following history: the patient was struck on the left eye by a bolt about ten years ago. Two years ago a growth began in the upper lid and thus steadily increased in size. At times the growth was painful. He had lost 30 pounds (13.6 Kg.) during the past three months.

On examination, I found a mass occupying the left orbit and part of the left cheek; it extended one-half inch anterior to the nose. The upper lid was stretched and entirely covered the bulb. The lower lid had been stretched by a mass from behind so as to expose the palpebral conjunctiva completely. The veins were much distended. The lids were almost purple. There was no ulceration of either lid. Near the inner canthus was a sinus which I took to be the lower canaliculus. The mass that occupied the orbit was fixed to the underlying structures but not to the skin; it was not painful to the touch. The cervical glands were not enlarged.



FIG. 14 (case 6)—High power magnification of carcinoma of the lacrimal gland

Stereoscopic pictures did not show evidence of increased vascularization of the skull. Exenteration was advised.

The roentgenologic report was that there was no evidence of bony tumor to be observed about the eye, and from the roentgenographic standpoint no other evidence could be observed than a large soft tissue mass occupying the orbital region (fig. 16).

Dr. Heninger of the medical service reported hypertension, heart disease, arthritis and arteriosclerosis associated with chronic nephritis.

Dr. Rosen reported that the auricular rate was 72, the ventricular, 72, the auriculoventricular interval, 0.16 second, and the Q-S interval, 0.07 second. There was sinus rhythm. No electrocardiographic evidence of myocardial disease was apparent.

Operation was performed on June 1, 1928. The tumor was circumscribed. The skin over the frontal bone above the supra-orbital ridge was retracted, as was the cheek below the infra-orbital ridge. As soon as this had been done I was able



Fig 15 (case 7) — Appearance of patient with melanoma of the orbit

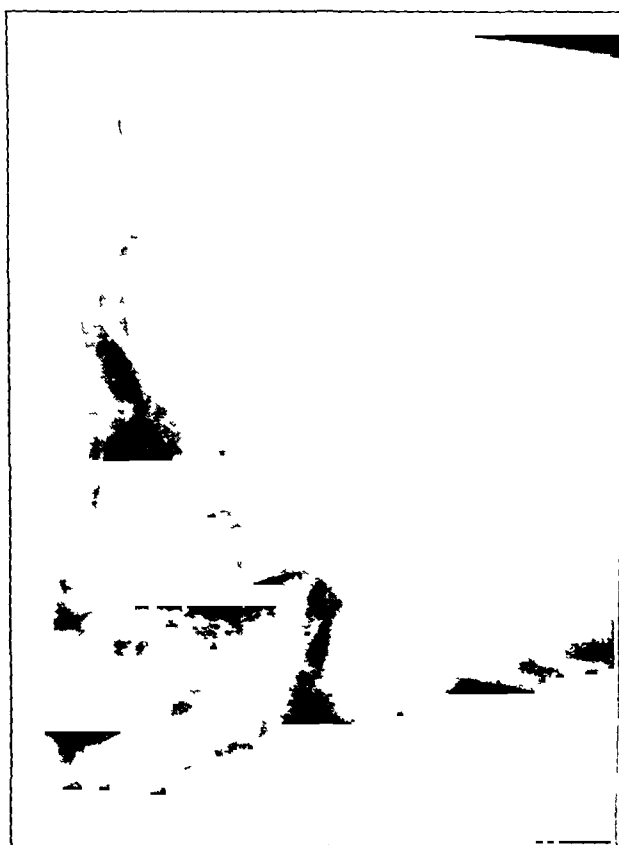


Fig 16 (case 7) — Roentgenogram of the skull showing melanoma of the orbit

to cut some of the muscular attachments which allowed mobilization of the orbital tumor

At this stage I realized that it was necessary to section the malar portion of the orbit, and this was done with a ronguer. About an inch of the external orbital rim was removed. The orbital tumor was mobilized, and the optic nerve and ophthalmic artery were sectioned. The tumor was removed, and a pack was introduced into the depths. At this stage, I saw that the orbital plate had been eroded and a portion of the frontal lobe of the brain could be seen in the upper portion of the wound.

The ophthalmic artery was ligated, the other vessels in the wound were transfixed. An iodoform gauze pack soaked in compound tincture of benzoin was introduced into the depths and three dermal sutures were used to make certain that the pack would remain in situ (fig. 17).



Fig. 17—Tumor removed from the orbit in case 7

Dr. Lanford reported that the specimen was a conical-shaped mass of tissue the base of which measured about 6 cm. in diameter and the mass about 9 cm. in height. The base presented a wide open palpebral fissure of both lids and a small amount of loose skin over the superior lid. The lid margins presented a few black cilia. The upper half of the palpebral opening was occupied by a spherical mass about 2.5 cm. in diameter the surface of which was covered by a pale gray wrinkled coat. Lying below and protruding farther than the upper mass was another spherical body nearly twice the diameter of the superior one and covered by a moist, pale yellow membrane probably the stretched lining fold of the conjunctiva sac. The sides of the mass presented a slightly regular appearance, being in general pink and covered with small shreds of bright red tissue. Toward the apex stumps of the blood vessels and nerves were encountered. In consistency the mass was generally firm though somewhat loose. The diagnosis was glioma of the optic nerve nonmetastasizing (figs. 18 and 19).



Fig 18 (case 7)—Appearance of melanoma of the orbit after sectioning

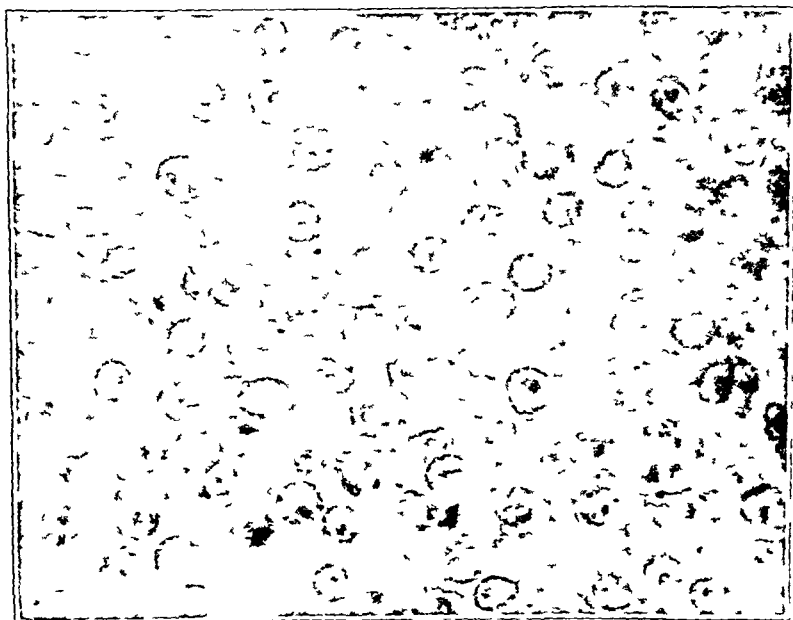


Fig 19 (case 7)—Microscopic view of section of tumor removed from the eye.



The patient left the hospital on June 18, 1928. He was kept under observation in his home town. He died during June, 1929.

During the last few months of his illness the patient developed a number of growths on the thoracic wall and on the back (fig 20). I was fortunate enough to obtain one of the tumors which had developed on the thoracic wall at a partial post-mortem examination done by the physician in attendance at the time of death. This specimen was submitted to Dr. Lanford, pathologist, who reported as follows:

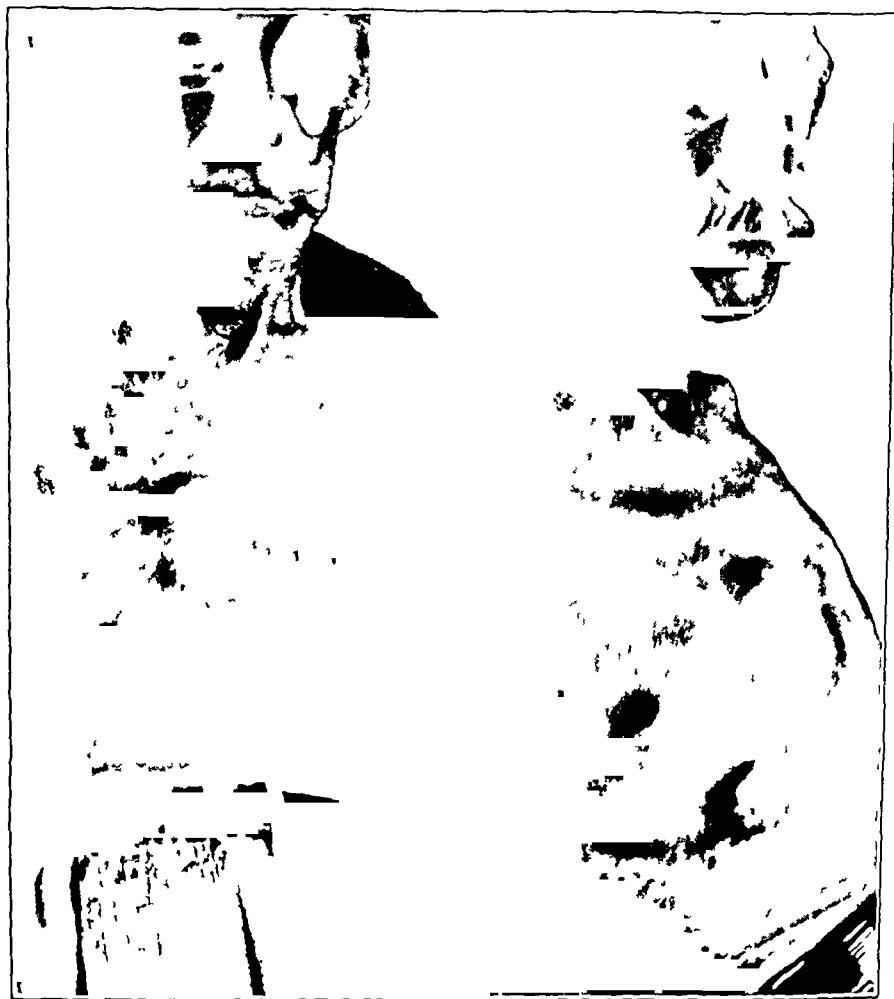


Fig. 20 (case 7).—Appearance of patient a few days before death, showing metastatic growths on the chest wall.

Examination of the nodule from the patient's chest showed it to be made up almost entirely of neoplastic cells of rather polygonal shape which in areas were held together by a stroma the origin of which it was not possible to determine. These cells were not definitely differentiating into the usual type of tissue such as carcinoma or sarcoma and had the histologic suggestions of melanoblasts but it was impossible to determine the formation of pigment, except that occasionally a few fine brownish granules were found. Dr. Lanford was inclined to look on the new growth as a melanoma (fig. 21).

The interest in this case was great prior to the development of the secondary growths the association of which with the primary growth Dr Lantord doubted originally

When I received the original report of glioma of the optic nerve, I was immediately interested in investigating the frequency of gliomas involving the orbital contents The more I investigated the literature, the greater were my doubts of the gliomatous nature of the tumor

In 1912 Curt Adams reviewed the cases of glioma of the retina that had been seen in von Michel's clinic in Berlin during twenty years He found that there had been one glioma of the retina for every 5832

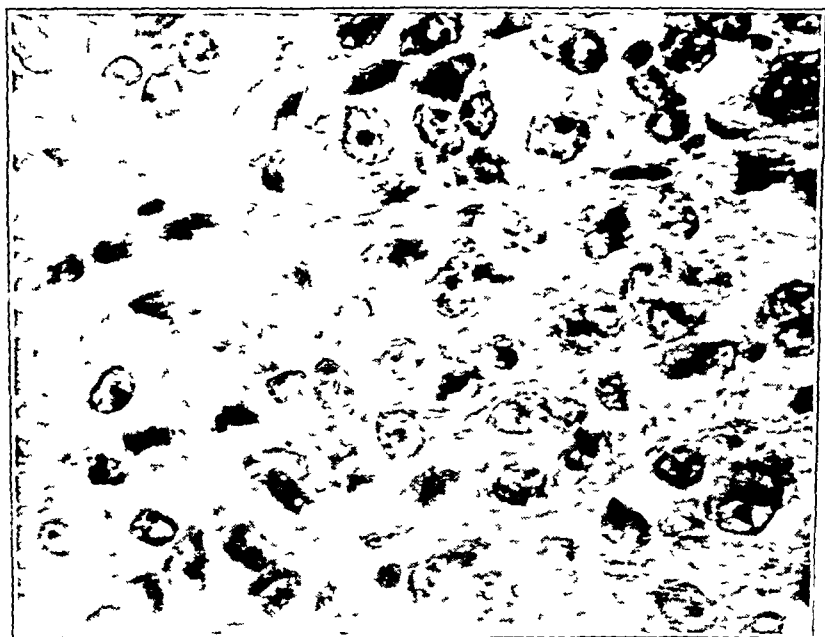


Fig 21 (case 7) —Section of nodule from the chest indicative of melanoma

patients Caspar reported finding only three gliomas in 40,000 patients with involvement of the eye Paul Berresford of London reported in 1916 the experience of the Royal London Ophthalmic Hospital during the past twenty-four years He found one glioma of the retina in 96,144 cases

From these statistics I was impressed with the extreme rarity of glioma of the retina

Curt Adams' report from von Michel's clinic stated that all the patients were less than 12 years old 94 per cent were under 4 years Berresford noted that 41 per cent of the cases occurred during the first year of life None of the patients was more than 6 years of age Ewing stated that glioma of the retina appears almost exclusively in

infants, 94 per cent were under 4 years of age. In the "Encyclopedia of Ophthalmology," it is stated that no true case has been found after the sixteenth year. These statements are bound to reflect some doubt on the diagnosis of glioma in our case.

In regard to the characteristics of gliomas of the optic nerve, I found the following statements in the literature which seem to me of value to one attempting to arrive at a differential diagnosis. The question may be asked: Does the tumor described meet the following requirements which were set up by various authorities with reference to glioma of the optic nerve?

In the "Encyclopedia of Ophthalmology" the following statement is made:

Gliomas of the retina (neuroepithelioma [Flexner]) are never pigmented. The mass is composed of small cells in a soft basement substance. The cells consist of nuclei surrounded by protoplasm in which minute processes are often found. *Some are glia cells, others are ganglion cells. It is a disease of childhood.*

Ewing, in his book on "Neoplastic Diseases," said:

Characteristic clinical behavior and peculiar structure render glioma retinæ one of the most striking examples of a specific tumor process.

The tumors grow expansively. *Metastases are late or absent*, but recurrence is common, and secondary growths appear in brain, skull, spinal cord, regional lymph nodes, and internal organs.

The essentially gliomatous character of these tumors appears in the presence of very many well formed neuroglia fibrils, which with specific stains are nearly always demonstrable and often form a very prominent structural feature.

According to Dr. James Ewing, who examined this tumor, there were no cells that he could consider glial cells.

Glioma recurs, but metastases are late or absent. The patient in question did not have a recurrence but did develop metastases. The secondary growths were classified as melanomas by Lanford.

Because of the existing doubt, Dr. Harold Cummins, a professor in the department of anatomy of Tulane University, was asked to examine the tumor with a view to determining, if possible, the embryologic origin of the growth. He reported that he found heavy pigmented cells within the eye which he took to be evidence of melanoma arising from choroid pigment cells.

Further investigation of the literature then revealed the following important facts with reference to orbital melanomas. Orbital melanomas are found in the conjunctiva, iris, choroid, sheath of the optic nerve and surrounding tissue. These growths are slow in their development. Histologically they may or may not contain pigment. The cells, according to Ewing, may be spindle shaped, round or polyhedral, appearing diffusely or in alveoli.

In view of the presence of pigmented cells in the tumor which occurred in a man past 70 years of age and later the development of a number of tumor masses on the surface of the body which histologically presented evidence of pigment-bearing cells it seemed desirable for Dr. Lanford to review the original growth and to submit this specimen to other pathologists for examination. Dr. Lanford after studying the

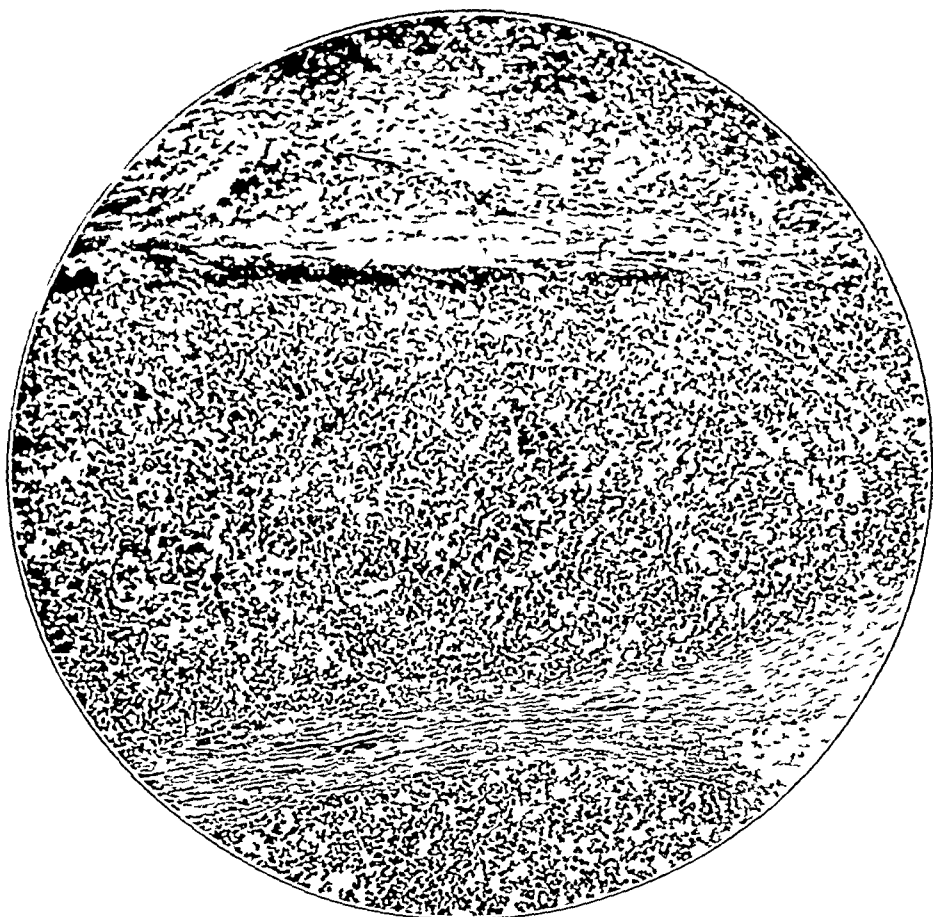


Fig. 22—Melanoma of the orbit (Ewing) in case 7

original growth in the light of the metastases, concluded with Drs. Ewing and Cummins, that the primary growth was a melanoma.

Dr. Lanford reported that he had reviewed the slides from the eye and had studied sections from other areas, and while his first interpretation of the pigment was that it was from the sclera, subsequent events had convinced him that it was the product of a growing tumor cell. He therefore believed that we were dealing with a melanoma probably in addition to a gloma.

A specimen of the original tumor was submitted to Dr. James Ewing, who examined it and reported that it was his opinion that the tumor was a "very cellular actively growing melanoma. It contains very little pigment, but the structure is typical. In the orbit, it is safe to assume that it arose from the choroid." In a subsequent communication he said, "I am quite unable to find any trace of glial tissue" (figs 22 and 23)

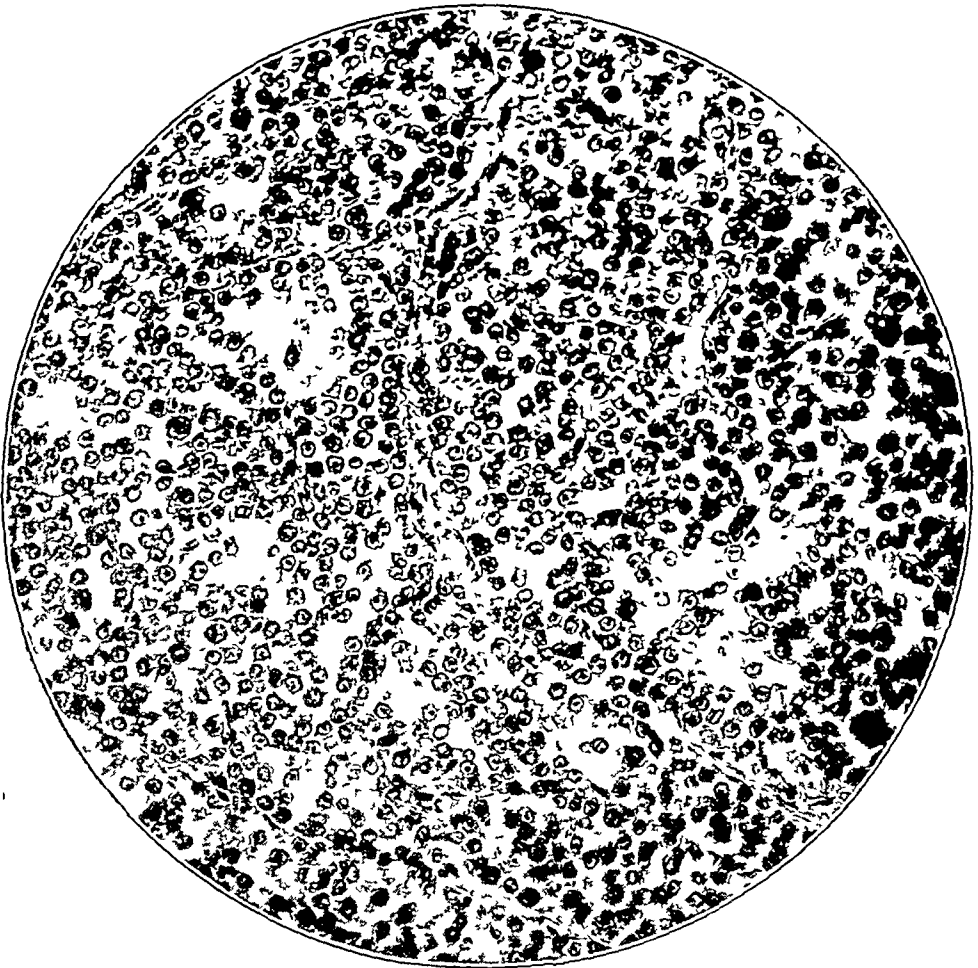


Fig. 23—Melanoma (Ewing) in case 7

This simplifies the entire problem, because it permits the acceptance of the secondary growths as metastases. The reporting of two unusual types of growths in the same person, particularly since the secondary growths appeared so soon after the removal of the original growth, would have been difficult to defend.

# TRAUMATIC PNEUMOCEPHALUS

## REPORT OF EIGHT CASES \*

CARL W. RAND, MD

LOS ANGELES

The term traumatic pneumocephalus<sup>1</sup> may be broadly used to designate the entrance of air into the brain or cranial cavity following a fracture of the skull. This air may produce a pocket in the substance of the brain itself, occupy the ventricular chambers, or less frequently disperse itself along the subdural spaces. In the great majority of cases the fracture of the skull involves one of the accessory nasal sinuses, most often the frontal. Cases, however, have been reported in which the line of fracture did not communicate directly with an air-containing sinus. The appearance of pneumocephalus may be immediate or remote. It has been known to develop within a few hours after the accident, on the other hand, instances have been reported in which it appeared from ten to seventeen months following an injury to the head. Whenever this condition is suspected clinically—as should always be the case in the presence of cerebrospinal rhinorrhea—roentgenograms should be made at once. The disclosure of a collection of air within the brain substance or the cerebral ventricles will give an immediate and graphic picture of the contingency to be met.

For many years it had been known that occasionally following an injury to the head with a fracture of the skull involving a sinus, air might pass through the outer wall of such a sinus under the subaponeurotic layer of the scalp, in which event an aerogenous tumor or tumors might form. Wernher<sup>2</sup> in 1873, reported such a condition. This extracranial form of pneumocranium more frequently follows a fracture in the mastoid region than one in the frontal sinus. Such accumulations of air under the scalp, however, must be exceedingly rare. I

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1. Many terms have been used to describe this condition, i. e., *aerocoele*, *pneumocoele*, *pneumatocoele*, *hydropneumatocoele*, *pneumocranium*, *hydropneumocranium*, *ventriculocoele*, *pneumoventricle*, etc. *Pneumocephalus*, however, seems to be the most logical. As Bullock pointed out, there is a certain analogy between *hydrocephalus* and *pneumocephalus* (*Traumatic Pneumocephalus*, *Surg. Gynec. Obst.* 43:750 [Dec.] 1926). *Hydrocephalus* not only describes a condition of "water on the brain," but has been a word familiar to physicians for many centuries. *Hydrocephalus* may be divided into the internal or external variety, depending on the position of the water. He argued that "a similar disposition is found to exist with air collections, which may with equal propriety be designated as internal or external pneumocephalus." It is recognized that pockets of air may be produced in the brain from infective organisms such as the *Bacillus aerogenes-capsulatus* of Welch or the colon bacillus, such conditions, however, are largely speculative and will not be considered in this paper.

2. Wernher. *Pneumatocoele crani*, *Deutsche Ztschr. f. Chir.* 3:381, 1873.

have never seen such a case although several examples of crepitant emphysema of the soft tissues about the face and eyes following fractures of the frontal sinuses have come to my notice. These extracranial forms of aerogenous tumors were usually treated by a simple pressure bandage, and healed spontaneously as granulation tissue filled in the defect in the bone. They are mentioned only as being analogous to the more common and more dangerous intracranial variety.

The roentgenogram has been chiefly responsible for the increased recognition of intracranial pneumocephalus. Before the advent of the roentgenogram, it was practically never diagnosed. In 1884, however, Chiari<sup>3</sup> recognized one of the first cases in a patient with a previous history of chronic inflammation of the ethmoid cells. The walls of these cells had been weakened and the dura eroded, so that following violent sneezing air was forced from a small rent in the dura connecting with the ethmoid cells into the frontal lobe and ventricles of the brain. At autopsy, he demonstrated the air pocket in the frontal lobe as well as the air in the ventricles, and argued that this collection of air had been present during life, explaining its entrance as a result of the explosive force of sneezing. Violent sneezing had been one of the outstanding symptoms which immediately preceded the onset of severe headaches, stupor and death.

The first case of traumatic pneumocephalus to be demonstrated by roentgenograms was one by Lockett,<sup>4</sup> in 1913. His patient had received a fracture of the skull involving the right frontal sinus. Roentgenograms taken at the time of injury revealed the fracture, but no air was apparent in the ventricles. The patient did well for some time, but on the nineteenth day he sneezed and apparently inflated the ventricles. He remarked to a friend, "I just sneezed, had a terrific pain in my head, and then a flow of a large amount of clear fluid came through my nose, about a cupful." Signs of increased intracranial pressure immediately followed, and subsequent roentgenograms of the skull showed the entire ventricular system, as well as a pocket in the right frontal lobe, to be distended with air. Recognizing the seriousness of this condition, Lockett at once performed a right subtemporal and a suboccipital decompression, removing the air both from the ventricles and from the cisterna magna. Meningitis, however, was already present and the patient died four days later, the air infiltrated ventricles being disclosed at autopsy.

Dandy,<sup>5</sup> in 1926, reported three new cases of traumatic pneumocephalus, collected twenty-five others from the literature, and gave an

3 Chiari, H. Ueber einen Fall von Luftansammlung in den Ventrikeln des menschlichen Gehirns, *Prag Vierteljahrsschr f Heilk* 5 383, 1884.

4 Lockett, W. H. Air in the Ventricles of the Brain Following a Fracture of the Skull. Report of a Case, *Surg Gynec Obst* 17 237, 1913.

5 Dandy, W. E. Pneumocephalus (Intracranial Pneumatocoele or Aerocele), *Arch Surg* 12 949 (May) 1926.

can do a review of the subject. He suggested a practical method of treating this condition by releasing the entrapped air, searching out the dural defect and closing the same either by a direct suture or a fascial flap transplant. His method of approach varied depending on the type of fracture and the position of the dural rent. Two procedures were suggested: (1) simple exposure of the fracture near the supra-orbital ridge and correction of the dural defect which lay directly beneath or (2) the use of an extensive frontal bone flap with search for the dural defect along the posterior wall of the frontal sinus or in the region of the ethmoid cells and closure of the same. Five years earlier Spiller<sup>6</sup> had discussed the treatment as follows:

The question of operation is a difficult one. If it is to be performed early it will be before any evidence of aerocele exists and will be done in the hope of preventing this lesion. It is not customary to operate on every case of linear fracture of the skull without displacement of fractured bone and without signs of intracranial pressure and it seems questionable whether operations would be advisable whenever the roentgen rays show a linear fracture permitting communication with air sinuses. In some instances it is difficult or impossible to be certain from roentgen ray examination whether an air communication with the interior of the cranium has been established. Presumably where such communication is shown by roentgen ray plates taken shortly after fracture has occurred operation might make closure of this communication possible and thus prevent the development of an aerocele and the possibility of the development of an aerocele must be considered in any case of fracture of the bones about the nose. It would be difficult to prevent the patient from blowing the nose and sneezing in the presence of such fracture but something might be attempted in this direction to lessen the danger.

Bromberg<sup>7</sup> in 1928 reported a case of typical frontal pneumocephalus with cerebrospinal rhinorrhea appearing seven weeks after a frontal fracture. He attempted to close the rent in the dura by the use of the roentgen ray but was unsuccessful. Following a suggestion of Israel Strauss the patient was placed in bed with his head held backward so that the nasal cavity would lie in a horizontal position. He was kept in this position for three weeks or more without turning his head every precaution being taken to prevent coughing, sneezing or straining. At the end of the month the air had practically disappeared from his brain and after two or three months he was entirely well.

In the traumatic form of pneumocephalus one has an initial cranial defect connecting with one or more of the paranasal sinuses or with the mastoid cells. It is well recognized that gaseous pressure may be increased in the paranasal sinuses by coughing, sneezing, straining, swallowing or the like so that it is much greater than that ordinarily

6 Spiller, W. G. Aerocele of the Brain. *M. Clin. N. Amer.* 5: 651 (Nov.) 1921.

7 Bromberg, W. Cerebrospinal Rhinorrhea with Pneumocephalus Secondary to Skull Fracture. *J. A. M. A.* 90: 2017 (June) 1928.



existing within the cranial chamber. Consequently, when there is a fracture connecting with such a sinus and the intracranial cavity by a dural rent, air may be forced from any of these sinuses into the brain substance itself. Connections with the frontal sinuses are most common, but cases have been reported in which the communication has been with the ethmoids (Chian,<sup>7</sup> Holmes,<sup>8</sup> Doyle<sup>9</sup> and Spiller<sup>10</sup>), the sphenoids (May<sup>10</sup> and Santoro<sup>11</sup>) or the mastoids (Duken<sup>12</sup> Teachenor<sup>13</sup> and Dandy<sup>14</sup>). The entrance of air into the brain and ventricles may be immediate, as was true in two cases of this series, but it more frequently happens from two to four weeks after the injury. Conversely, a pocket of air may exist in the substance of the frontal lobe for many months without breaking through into the ventricle.

Several factors favor the frontal region as the most common site for the development of pneumocephalus. Fractures frequently occur in the frontal sinuses, and the dura in this region is thin and very tightly adherent to the skull. A fracture of the inner wall of the sinus is only too prone to cause a rent in the dura as well. There is usually a contusion or laceration of the frontal lobe in the immediate proximity of the fracture, consequently adhesions tend to form, walling off the bruised brain at the point of fracture from the surrounding subdural space. Ideal conditions are therefore produced for the passage of air directly from the sinus into the brain substance, if by chance the pressure within the sinus itself is suddenly increased. Hence coughing, sneezing, straining or anything that will raise the gaseous pressure within the sinus is most often the immediate predecessor of the entrance of air into the brain or ventricles.

Dandy called attention to an unusual condition of the sinus which not infrequently exists. The size or character of the sinus may be such as to permit the outflow of spinal fluid as seen in cerebrospinal rhinor-

8 Holmes, G. W. Intracranial Aerocele Following Fracture of the Frontal Bone, *Am J Roentgenol* **5** 384 (Aug) 1918.

9 Doyle, A. S. Traumatic Pneumocranium, *Am J Roentgenol* **8** 73 (Feb) 1921.

10 May, R. J. Report of a Case Showing Air Within the Cranial Cavity, *Am J Roentgenol* **6** 190 (April) 1919.

11 Santoro. Rinorrea cefalo-rachidiana e pneumoventricolo spontanei da tumore della base (ipofisi?), (Spontane Liquorrhinorrhoe und Pneumoventrikel bei einer Basis- (Hypophysen-?) (Geschwulst), *Riv oto-neuro-oftalmol* **1** 484, 1924.

12 Duken. Ueber zwei Falle von intracraneller Pneumatocele nach Schussverletzung, *Munchen med Wchnschr* **62** 598, 1915.

13 Teachenor, F. R. Pneumoventricle of the Cerebrum, *Ann Surg* **78** 561 (Nov) 1923.

14 Dandy, W. E. The Treatment of Staphylococcus and Streptococcus Meningitis by Continuous Drainage of the Cisterna Magna, *Surg Gynec Obst* **39** 760 (Dec) 1924.

open but is adapted to allow the escape of the entrapped air. It has been stated that a ball valve action may exist along the sinus tract which will permit entrance of air into the cranial chamber but which prevents its exit. Cases have been reported in which the entrance of air was apparently simultaneous with the stoppage of cerebrospinal rhinorrhea. This however does not necessarily follow as cases have been known in which signs of meningitis appeared as soon as the cerebrospinal rhinorrhea stopped, no air being present within the cranial chamber. The reverse however is more frequently seen.

The symptoms may be sudden or gradual, violent or mild, depending largely on the amount of air and the rapidity of its entrance into the cranial chamber. Usually the appearance of pneumocephalus is shown by the occurrence of headache, nausea and vomiting, in short the signs of increased intracranial pressure appear. The patient may show evidences of drowsiness and stupor and even go into coma. Mental changes in the form of disorientation, forgetfulness or even delusions may occur. A choked disk may or may not develop. Convulsions have occurred and may be of the jacksonian type. Not infrequently there will be chills and fever with the characteristic signs of a rapidly developing meningitis. Stiffness of the neck and a positive Kernig sign are the rule. Even in cases in which actual meningitis is not present symptoms of mild meningeal irritation are seen. These gradually pass away as the patient recovers.

The presence of cerebrospinal rhinorrhea especially following an attack of sneezing or coughing is regarded by Dandy <sup>5</sup> as almost pathognomonic of pneumocephalus. He stated "A cerebrospinal fistula is probably the sign of greatest significance. Its presence should always make one suspect pneumocephalus. When sneezing follows a frontal fracture with rhinorrhea the suspicion grows stronger, but when sneezing is followed by a flow of cerebrospinal fluid one could almost be safe in making a positive diagnosis of pneumocephalus without the roentgen ray."

#### REPORT OF CASES

*CASE 1—Depressed right frontal fracture followed by immediate traumatic pneumocephalus. Elevation of depressed fracture on same day. No attempt made to remove air. Gradual absorption of same, and recovery of patient.*

A. A. aged 23, a Mexican laborer, was injured on Dec. 5, 1919, when he was struck in the right frontoparietal region by a falling piece of a 2 by 4 timber and was immediately rendered unconscious. He was first taken to the Ramona Hospital in San Bernardino, then transferred to the Good Samaritan Hospital in Los Angeles. At the time of his entrance to the latter hospital, he was found to be suffering from an extensive compound comminuted, depressed fracture of the right frontal region. Brain substance was oozing from the laceration in the scalp into his hair. He was in deep coma and having frequent convulsions. He was taken to the operating room where Dr. Shoemaker elevated the depressed fragments. At the time it was noticed that bubbles of air came through the



Fig 1 (case 1)—Postoperative roentgenogram taken several hours after injury, showing a large pneumocephalus of the right frontal lobe. Apparently the dural defect was inadvertently closed at operation as the pneumocephalus absorbed and did not recur.

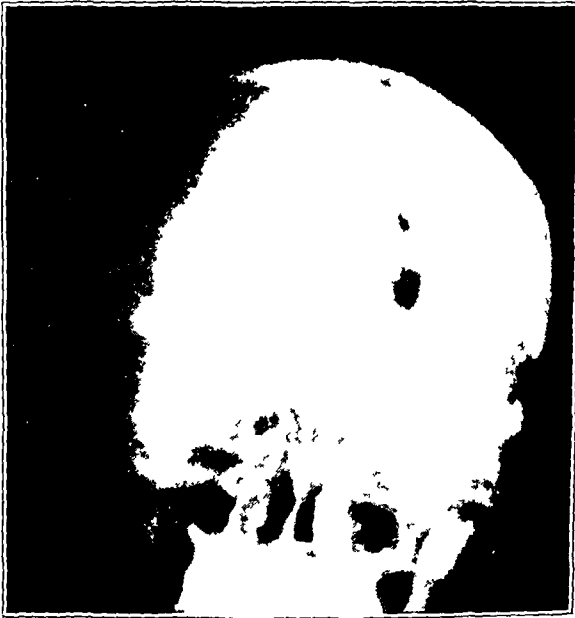


Fig 2 (case 1)—Roentgenogram taken a few hours after operation, showing corrected fracture of the right frontal bone as well as air in the right frontal lobe and partial filling of the ventricle, this air was absorbed spontaneously.



At the time of my examination on May 3, the man was exceedingly ill and in deep coma, the temperature was 104 F., pulse rate, 200 and respirations, 40. He was bathed in perspiration, there was marked rigidity of his neck, a double positive Kernig sign, marked swelling and edema of both eyelids and the tissues about the forehead were boggy. Brain substance oozed from a recent stab wound just above the bridge of the nose. The pupils were unequal and fixed, the right being larger than the left, the eye grounds showed marked congestion of both fundi and haziness of the disk margins. All superficial and deep reflexes were in abeyance. The white blood cell count was 43,000, the polymorphonuclears, 85 per cent.

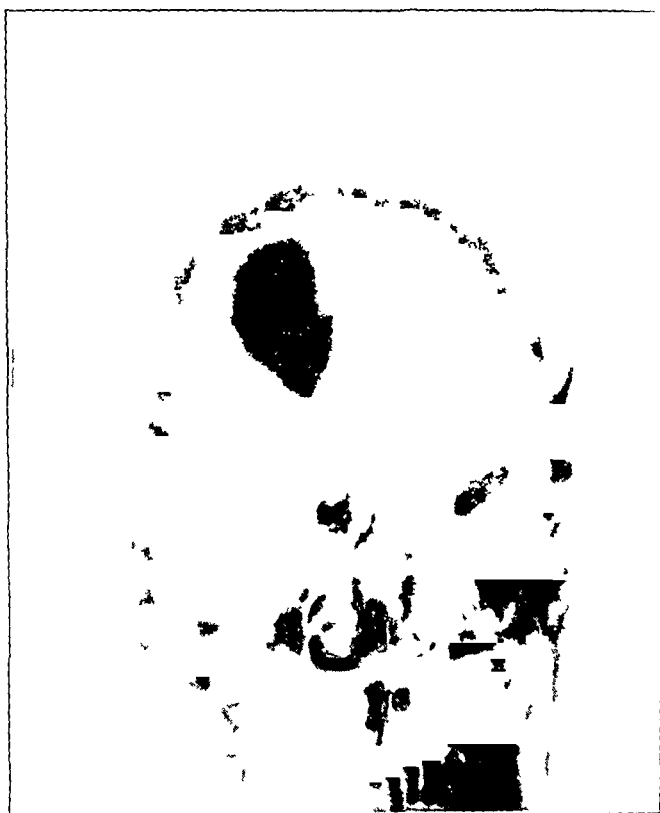


Fig 4 (case 2) —Roentgenogram taken approximately one month after injury, showing defect in the frontal bone from removal of depressed fragments and a pocket of air in the right frontal lobe

Roentgenograms of the skull taken at this time revealed a comminuted fracture of the right frontal bone, with a large defect where fragments had been removed, and a large pneumocephalus in the right frontal region (figs 4 and 5). A spinal fluid examination at this time showed the fluid under great pressure, containing many gram-positive organisms, probably pneumococci. The patient died on May 5, and the coroner reported that death had been caused by depressed fracture of the skull and acute meningitis.

*CASE 3—Depressed right frontal fracture followed by fever and slow convalescence. Five weeks later, signs of meningitis and traumatic pneumocephalus*



Fig 5 (case 2) —Roentgenogram taken one month after injury, showing a large pocket of air in the right frontal lobe. Point of communication of the air pocket with the region of the frontal sinus indicated by arrow.

Roentgenograms of the skull taken on March 9, revealed a rather extensive Y-shaped fracture in the right frontal region. At the fork of the Y one could see a triangular piece of bone which was slightly depressed, but no air was present. The patient had an intermittent fever from the first, and there was a serous discharge from his right ear which may have been spinal fluid. About the middle of April, 1927, he began to get worse.

On April 22 he was found lying on his left side. He refused to turn on his back because of pain in his head and neck. The neck was quite stiff, and there

was a double positive Kernig sign. There was a healed scar in the right fronto-temporal region. The pupils were unequal, the right being considerably larger than the left, both reacted well to light and distance. There was a complete peripheral facial paralysis on the right. The discharge from the right ear had ceased. The eye grounds were within normal limits, save for some congestion of the retinæ and vessels. The deep reflexes were all present and equal, except the left knee jerk, which was quicker than the right. There was a positive Babinski sign on the left, a negative on the right. An examination of the spinal fluid showed a slightly cloudy fluid under pressure which contained 152 cells per cubic millimeter and reacted positively to the Noguchi test and negatively to culture. Examination of the blood showed hemoglobin, 75 per cent, erythrocytes, 4,440,000, leukocytes, 10,350, color index, 0.9, polymorphonuclears, 80 per cent, large mononuclears, 18.5 per cent, transitional leukocytes 1.5 per cent.

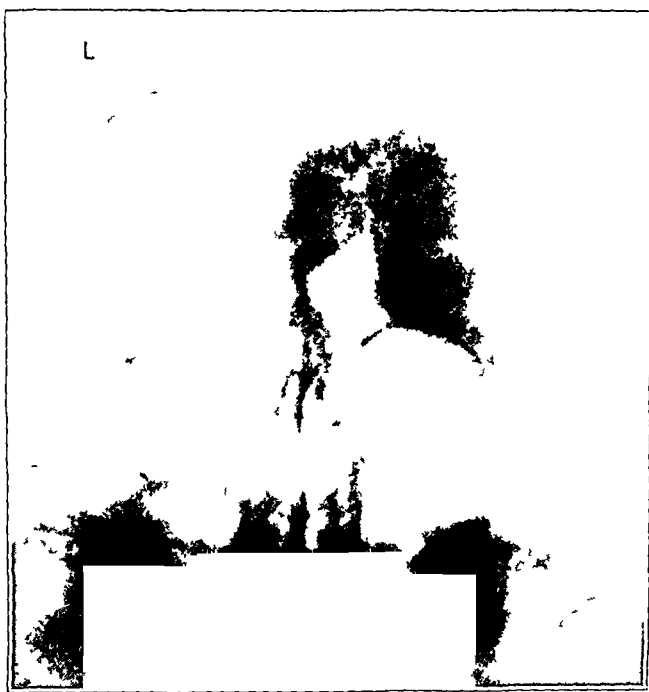


FIG. 6 (case 3).—Roentgenogram taken approximately six weeks after injury, showing air in the right frontal lobe and practically filling the ventricular system, postero-anterior view.

Roentgenograms of the skull taken on April 22 revealed an old fracture in the right frontal region. The entire ventricular system was filled with air (fig. 6). In the right frontal lobe just in front of the anterior horn of the ventricle one could see a pocket of air. It was evident that the patient had developed a traumatic pneumocephalus, the air coming through the right frontal sinuses. It seemed advisable to try to empty the air from the pocket and ventricles, and if possible close the opening in the dura.

At operation, the fracture line in the right frontal bone was exposed. On rongeur-ing the bone, bubbles of air escaped between the dura and the inner table of the skull. The dura was at least four times its normal thickness. The surface of the frontal lobe showed inflammation with exudate and thickening of the pia



Fig 7 (case 4) —Roentgenogram taken approximately four weeks after injury, showing a large pocket of air in the left frontal lobe and partial filling of the lateral ventricle

C W, aged 19, single a laborer, was referred by Dr Wallace Dodge of Los Angeles on April 21 1928. He was injured on March 29, 1928, when he was struck in the midforehead just below the hair line, by a falling piece of timber. He was unconscious for a very short time. A roentgenogram taken at the Methodist Hospital on the date of his injury showed a linear fracture in the left frontal bone, which ran into and involved both walls of the left frontal sinus. The patient presented no unusual neurologic signs or symptoms during the next two weeks, and at the end of this time was allowed up in a wheel chair. On April 15 he began to have a headache and to vomit. The headache and vomiting continued daily for the next week.



At the time of my first examination on April 21, he was mentally clear and conscious. The scar in his forehead was healed and clean. The neck was a little resistant, and a Kernig sign was suggestive on both sides. The eyegrounds were normal, and the pupils were equal and reacted well to light and distance. Otherwise, the results of the neurologic examination were negative. It was felt at the time that there was a suggestion of increased intracranial pressure, possibly in extension of infection from the frontal sinus, a traumatic pneumocephalus was not considered, but a brain abscess was thought likely. On April 26, roentgenograms of the skull were again made, and a large pocket of air was disclosed within the substance of the left frontal lobe (fig 7). The lateral ventricles

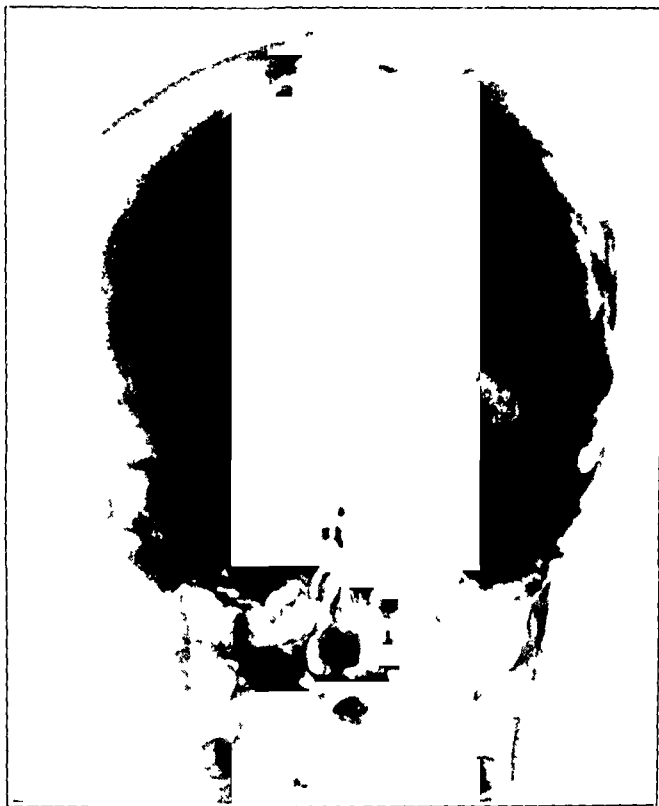


Fig 8 (case 4) —Roentgenogram taken about five weeks after injury showing a pocket of air in the left frontal lobe communicating with the region of the left frontal sinus, the lateral ventricles are also filled

were also filled with air (fig 8). One could see a direct communication of air from the posterior wall of the left frontal sinus into the pneumocephalus. It was felt advisable to keep the boy absolutely quiet in bed, warning him against coughing or sneezing, and not permitting him so much as to raise his head. No cerebrospinal rhinorrhea was present. This treatment was carried out for two or three days with fair relief from headache and vomiting, when the symptoms again recurred, and an exploration was advised.

On May 2, a left frontal osteoplastic flap was turned down according to the method of Dandy. The dura was found to be very tense, and the flattened convolutions of the frontal lobe could be seen shining through. The dura was nicked, and a ventricle needle was introduced into the air pocket beneath. This



was learned that she fell downstairs, striking her head on some hard object. When admitted to the hospital she was in a semicomatose condition, there was ecchymosis about both eyes, which were swollen shut, and the forehead was puffy with a laceration near the midline. Palpation revealed a depression of the bone in the midfrontal region. The pupils were equal and reacted well to light and distance, the eyegrounds were within normal limits. There was no bleeding from the ears, but profuse bleeding from the nose. The results of the neurologic and physical examinations were essentially negative.

A roentgenogram of the skull taken on May 17 revealed a much comminuted fracture in the frontal region involving the anterior fossae on both sides. Several

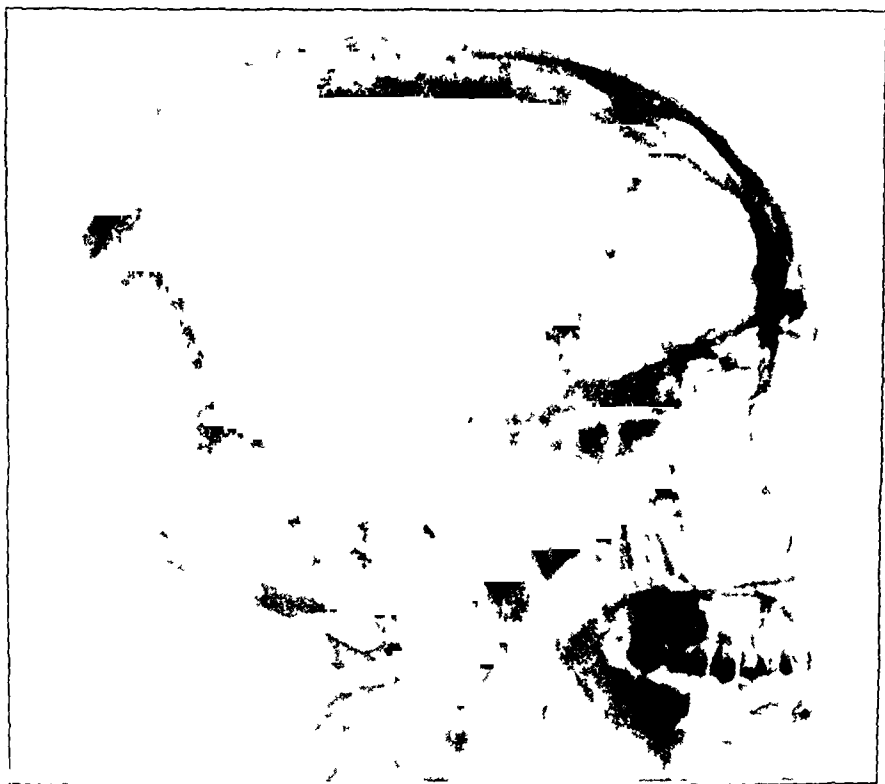


Fig. 10 (case 5)—Roentgenogram taken approximately a month after injury showing a large pneumocephalus in the right frontal lobe. The fracture lines can be faintly made out. Roentgenograms taken immediately after injury failed to show the presence of air in the cranial cavity.

comminuted fragments appeared to project into the cranial vault in the anterior fossa near the superior external angle of the right side. No air was present in the cranial chamber.

After a few days, the patient's condition cleared up satisfactorily except for rather severe headache. She did not have a cerebrospinal rhinorrhea at any time. She refused to have the depressed fracture elevated, and left the hospital of her own accord on May 29.

She returned on June 15, 1928, very ill. At this time she had a fever of 102.6 F, pulse rate 120, respirations 20, a stiff neck and a double positive Kernig sign. She was delirious part of the time, restless and resisted examination, had

the fracture line was visible on the right side. The eye on the right side was closed and the eye on the left side was open. The fracture line was visible on the right side and the eye on the right side was closed. There was a large collection of air in the right frontal lobe.

A large collection of air in the right frontal lobe was removed. The plebium was greatly increased and the fracture line was visible. The cell count showed 4320 cells per cubic millimeter, 85 per cent which were polymorphonuclears and 5 per cent lymphocytes. A Gram stain showed a few gram positive extracellular diplococci containing gas in the right frontal lobe. This was a continuation.

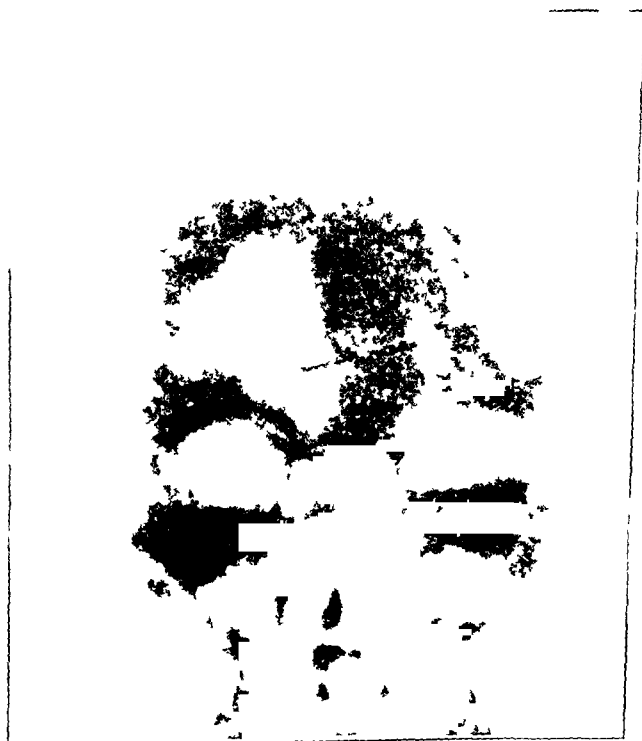


Fig 11 (case 5) —Roentgenogram taken approximately one month after injury showing a large collection of air in the right frontal lobe. Extensive fracture lines in the frontal region can be well seen.

Pneumocephalus was suspected and roentgenograms were again taken on June 18. These revealed a large collection of air in the right frontal lobe, the comminuted fracture of the skull in the frontal region extending into the anterior portion of the anterior fossae on both sides was again seen (figs 10 and 11). There was overlapping at the median transverse side of the fracture, giving an appearance of some depression of the upper fragment and some outward displacement of the lower fragment.

She was operated on June 20, when a flap of liberal size was turned down in the right frontal region. The dura was under great tension. This was opened and a pneumocephalus in the right frontal lobe was emptied of air by a ventricle needle, the air coming out under great pressure. The dura was then lifted from

the floor of the anterior fossa, and two rents were discovered. Through one of these, a pointed spicule of bone had penetrated from the frontal sinus. This rent was sutured. A second rent was found deep down over the cribriform plate at a point where suture of the dura was impossible. Consequently, a piece of muscle and fascia lata were removed from the left thigh, and the defect in the dura was closed with them. The depression in the frontal bone was corrected, and the wound closed tight. Convalescence was stormy. By June 26, all air had disappeared from the cranial cavity, as was revealed by subsequent roentgenograms. The patient continued to have headaches and signs of meningeal irritation, and lumbar punctures were made from time to time. She was given methenamine intravenously, as much as 90 grains (5.8 Gm.) a day being given for short periods of time. From the time of her second admission, until her discharge, she was given 1,920 grains (124.4 Gm.) intravenously. The kidneys were watched closely and apparently suffered no ill effects. It could not be definitely proved whether formaldehyde was transmitted in the spinal fluid. Lumbar punctures were repeated from time to time and the results were as follows. On June 23, 10 cc of fluid was removed, it was cloudy and contained 1,650 cells per cubic millimeter. The globulin was increased. A few extracellular gram-positive diplococci were seen. These may have been due to a contamination. On July 4, 65 cc of fluid was removed, it was turbid, and under increased pressure and contained 1,650 cells per cubic millimeter. Smears or cultures were not made. On July 10, 75 cc of fluid was removed, it was turbid and under increased pressure and contained 1,520 cells per cubic millimeter. On July 20, 100 cc was removed, it was clear but yellowish and contained 1,285 cells per cubic millimeter, which were mostly lymphocytes. It was noted that the patient seemed better when spinal punctures were not made, consequently, no further punctures were carried out.

During the first weeks after the operation, the patient was noisy, delirious and very difficult to handle, in fact, she had to be put in the psychopathic ward for a time. Gradually her condition cleared up, and by August 14, she had apparently completely regained her mental faculties, the wound was well healed and she was discharged from the hospital. Correspondence with her from time to time since reveals that she remains in good health.

*CASE 6—Occipital and questionable right frontal fracture, with immediate cerebrospinal rhinorrhea and pneumocephalus. Six days later sudden stoppage of rhinorrhea and appearance of signs of acute meningitis, disappearance of air at this time. Death from pneumococcus meningitis.*

C. S., aged 41, married, a carpenter, was referred by Dr. A. W. Moore of Los Angeles. He was injured at 10:30 a. m. on May 21, 1928. In attempting to loosen some bolts from the top of a door, he in some way received an electric shock and fell 20 feet. He was not rendered unconscious, but sustained a Colles fracture of the left wrist, minor burns on fingers of the left hand and a fracture of the skull in the right frontal region. There was profuse bleeding from the nose and mouth and a marked cerebrospinal rhinorrhea which began at the time of the accident and stopped suddenly on May 27, six days later. As long as the rhinorrhea continued, the patient's mind was clear and he was conscious, but he had considerable headache. The leakage of fluid stopped about 2 p. m., his headache became excruciating, and he dropped into coma two hours later, his temperature rapidly rising to 104 F.

Roentgenograms of the skull taken on May 21 (the date of injury) showed an unusual condition. There was practically complete filling of the left ventricle of the brain with air, which also was present in the subarachnoid space over the entire brain (figs. 12 and 13). No air was seen in the substance of either frontal lobe. There was a linear fracture in the right occipital region below the lambdoid

suture and a second line near the outer angle of the eye on the right side which resembled a fracture. Roentgenograms taken on May 28 showed that practically all the air had been absorbed. This, however, did not influence the course of his meningitis.

The patient was first seen by me on May 28, 1928, two days before his death, at which time the right eye was discolored and swollen and the neck stiff, and he had a positive Kernig sign on each side. Divergent squint was present. The right pupil was static and a little larger than the left, the left reacted sluggishly. He was apparently blind in the right eye. The eye grounds showed marked congestion of the disks, with beginning choking on each side. Respirations were of the Cheyne-Stokes type, the temperature was 104 F., pulse rate, 80, white blood



Fig. 12 (case 6) —Roentgenogram taken on day of injury showing extensive filling, both of the ventricles and subarachnoid spaces with air. This is the only case in which the subarachnoid spaces filled with air.

cells, 9500, and polymorphonuclear cells 68 per cent. A lumbar puncture performed on May 28 showed a spinal fluid under a pressure above 300 mm., and a cell count of 14,000 per cubic millimeter. Gram stain of sediment showed numerous pus cells and a moderate number of gram-positive lanceolate diplococci, some intracellular. Culture showed a pure growth of pneumococcus, group IV. Death occurred on May 30, 1928.

This case differs from the others reported with the exception of case 1 in that pneumocephalus developed immediately on the day of injury, as shown by the early roentgenograms. As long as the cerebro-spinal fluid leak continued the patient was fairly comfortable. As soon as this stopped he lapsed into coma and died shortly afterward. Before death the air had disappeared from the ventricles.

and subarachnoid spaces. The definite source of entrance of the air and micro-organisms in this case was not determined.

*CASE 7—Extensive comminuted bilateral frontal fracture communicating with the right frontal sinus. Cerebrospinal rhinorrhea developing about a week later. Appearance of headache, mental hallucinations and discovery of traumatic pneumocephalus about six weeks after injury. Operative closure of dural defect by muscle graft. Recovery.*

J. H. I., aged 44, married, a business man, was seen in consultation with Dr. H. D. Newkirk of Santa Ana on June 11, 1929. On May 6, he sustained an



Fig. 13 (case 6)—Roentgenogram taken on day of injury showing air in the lateral ventricles and a large collection in the subarachnoid spaces.

extensive fracture of the skull in the frontal region. The circumstances surrounding his injury were not clear. He was found in a basement, unconscious, with lacerations of the scalp, especially in the left frontal region, and a fracture of his left elbow. There was no bleeding from his ears. After a day or two his condition began to clear up, and improvement continued until June 9.

Roentgenograms of the skull taken soon after the accident showed an extensive fracture in the frontal region. There was a very small depression in the left temple just outside of the orbit, this depression measured approximately 1 by 1.5 cm, and was pushed down about 0.5 cm. There were other fracture lines run-

ning across the frontal bone one communicating with the right frontal sinus. No air was seen inside of the cranial cavity.

On June 9, he exhibited his first delusions. He insisted that his wife was with him and that she was taking care of him. As a matter of fact, she was 500 miles away. He also became confused and disoriented. He did not know where he was or that he was in a hospital. He lost all interest in his business, never inquired about it and showed no worry regarding it. This was quite different from his normal mental attitude.

On examination on June 11, the patient appeared to be in good general physical condition. There were two recently healed scars on the left side of the forehead.

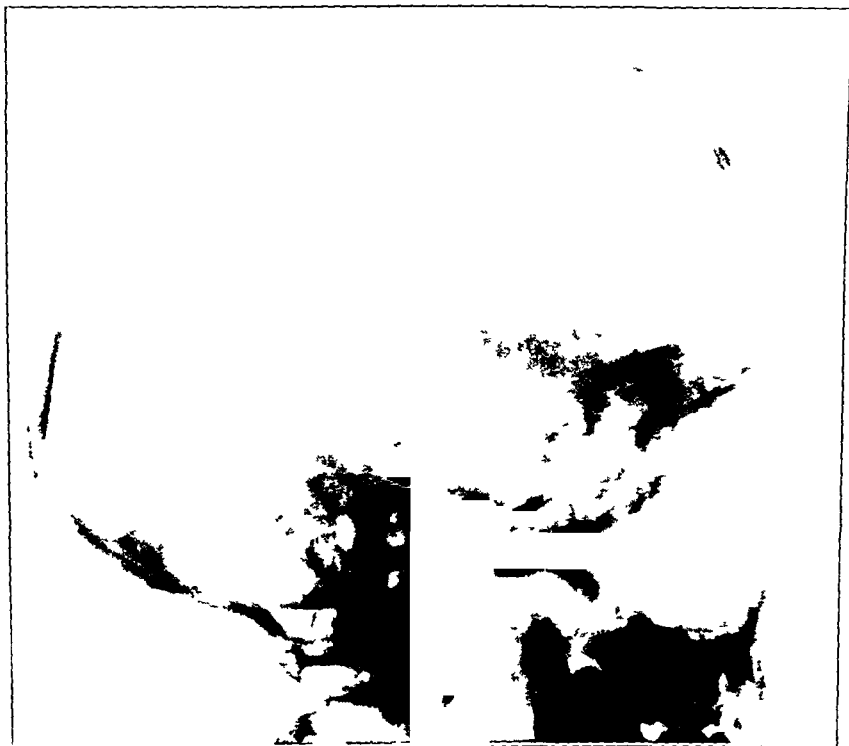


Fig. 14 (case 7).—Roentgenogram taken approximately seven weeks after injury. A tremendous pneumatocele is evident in the right frontal lobe as well as the presence of air in the lateral ventricle. The fracture lines can be made out in the frontal bone.

In the left temple, just outside of the orbit, one could feel a very slight depression in the bone. The cranial nerves were normal, and the eye grounds appeared to be within normal limits. There were no abnormal reflexes or the Babinski group nor ankle clonus on either side. He used all extremities well.

Laboratory examinations showed the urine and Wassermann reaction of the blood to be negative. The blood count showed hemoglobin 84 per cent, red blood cells, 4,610,000, color index 0.93, white blood cells 10,200, polymorphonuclears 70 per cent, lymphocytes 27 per cent, mononuclears 3 per cent, blood grouping II.



The patient seemed quite well oriented on the day of this examination. He knew that he was in a hospital at Anaheim, gave the day of the week and month correctly and discussed his business in some detail. He performed the 100-7 test very quickly and accurately and seemed mentally himself, except for one delusion. He insisted that his wife was in the hospital with the two children, and he could not be persuaded otherwise. As already stated, she was at their home 500 miles away.

About this time a cerebrospinal rhinorrhea was observed, the exact time of its development is not known. After his recovery the patient said that it started within a week from the date of his injury, but it was not conspicuous until a

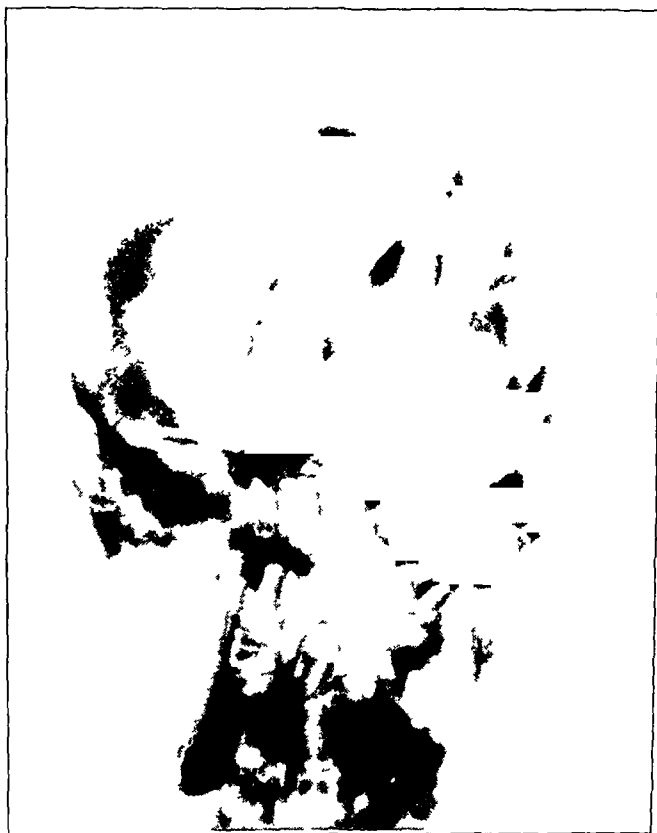


FIG 15 (case 7) —Roentgenogram showing multiple fracture lines and a large collection of air both in the right frontal lobe and filling the ventricular system

month later. The fluid came from the right side of his nose and in large quantities. He also developed considerable headache. At times his headache was very severe, at other times he was apparently free from pain. When the headache was present, he was usually badly confused as to time and place. When the headache was absent his mind, for the most part, was clear. Abstracts from a letter written on June 16, 1929, will perhaps give an idea of his mental condition.

'Anaheim Asylum

Anaheim, Oct 17, 1929 (Correct date June 16, 1929)

Your letter enclosing the dried peaches and dried fruit bag arrived this morning early. Every thing in it were fine. The fruit was fine also.

Our paper and stamps are getting low so we take advantage of writing on the other fellows paper etc

I did not do that today because I did not hear that the box contained so much stuff so direct from San Meiojoioinhrjones's"

He was brought to Los Angeles on June 26 when he was found to be in a very confused condition. Roentgenograms of the skull were taken again at this time as a traumatic pneumocephalus was suspected. These plates showed a tremendous collection of air in the right frontal lobe and filling the lateral ventricles (figs 14 and 15). The patient was operated on two days later, a right frontal bone flap being turned down. On reflecting the flap to our surprise the dura had collapsed and it was apparent that the pneumatocele had emptied itself. On reflecting the dura from the back of the right frontal sinus a fracture in the



Fig 16 (case 8) —Roentgenogram taken twenty-two days after injury showing a large pneumatocele in the right frontal lobe. A roentgenogram taken two days after injury failed to show air in this region.

posterior wall was disclosed and a corresponding rent in the dura was found. This rent measured approximately 1 cm. in length. It was not feasible to attempt repairing it by direct suture, fascia lata and muscle grafts being used for this purpose. He stood the operation well but showed considerable mental confusion the following day. In short, for approximately two weeks he had periods when he was badly confused. He usually thought that he had been at home and had returned or that there had been visitors other than the people who had actually called. Mental confusion occurred at times during the rest of his stay in the hospital. He returned to his home on August 11.

CASE 8—Extensive compound comminuted depressed frontal fracture extending into the right frontal sinus and orbit. Depressed fracture of the anterior

*of injury Appearance of cerebrospinal rhinorrhea, and traumatic pneumocephalus three weeks later Operative closure of dural rent with muscle and fascia lata Recovery*

C E E, age 19, a messenger boy, was admitted to the Los Angeles General Hospital on July 5, 1929. A few hours earlier he had been injured in a collision between his motorcycle and an automobile. He was unconscious only a few minutes. At the time of admission his mind was perfectly clear. Examination revealed an extensive laceration crossing the forehead. Under this was a large depressed fracture of the frontal bone. The right eye was swollen shut. He was

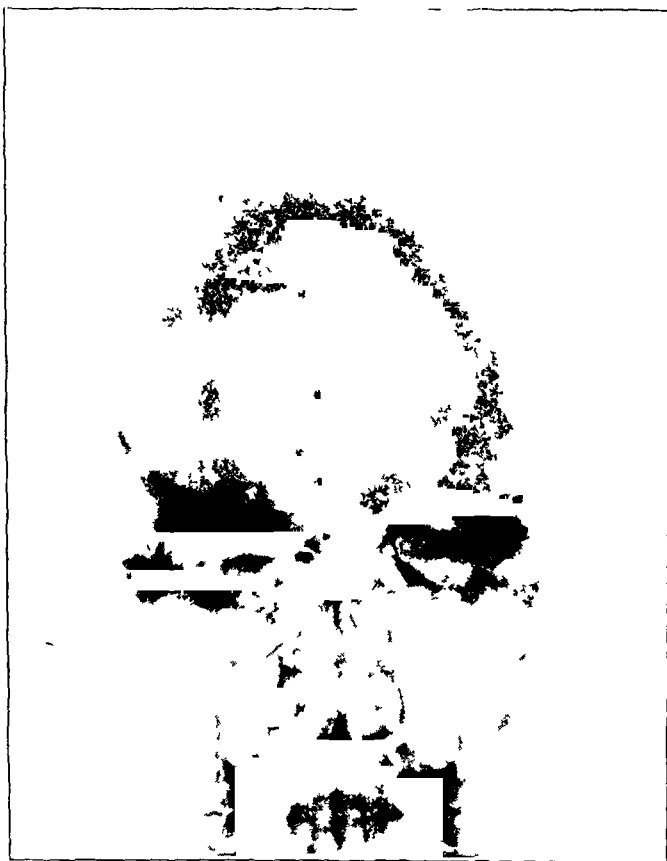


Fig 17 (case 8) —Roentgenogram taken twenty-two days after injury showing frontal fracture and pneumatocele in the right frontal lobe. The point of communication with the frontal sinus can be plainly seen.

taken to the operating room and the depressed fragments were brought up into place. The wound healed without infection. Within a few days, it was apparent that he was blind in the right eye, the pupil being widely dilated and failing to react to light. Examination of this fundus showed an enormous hemorrhage covering the nerve head and extending well into the macular region. The retina did not appear detached. The left fundus appeared normal.

A roentgenogram of the skull taken on July 7, two days after operation, showed a large irregular fracture of the frontal bone, involving the right frontal sinus. The fragments were in good position.

For the next three weeks the patient did quite well except for recurrent nose-bleed. No cerebrospinal rhinorrhea was noted. A complete ptosis of the right eyelid had developed, and an enophthalmos of the globe was apparent.

On July 26 he was transferred to the Santa Fe Hospital. About this time, cerebrospinal fluid began to leak through the right nostril. He also complained of considerable headache. The ptosis of the right eyelid began to disappear, but

*Data on Eight Cases of Traumatic Pneumocephalus*

Case	Age	Sex	Type and Location of Fracture	Duration of Time Following Injury Until Appearance of Pneumocephalus	Location and Extent of Pneumocephalus	Operative Procedure	Result
1	23	M	Depressed right frontal	Pneumocephalus appeared on day of injury	Right frontal lobe; ventricles partially filled	Fracture elevated; pneumocephalus discovered at operation; gradual absorption of air	Recovery
2	24	M	Depressed right frontal	Immediate appearance of cerebrospinal rhinorrhea; pneumocephalus developed four weeks later	Right frontal lobe	Not operated; pneumococcus meningitis developed	Death
3	13	M	Depressed right frontal	Pneumocephalus developed after five weeks together with meningitis	Entire ventricular system and right frontal lobe	Fracture elevated; rent in dura not found; streptococcus meningitis demonstrated	Death
4	19	M	Linear left frontal sinus	Pneumocephalus appeared after four weeks	Left frontal lobe; lateral ventricles	Explored; rent in dura repaired by suture and fascia lata graft	Recovery
5	23	F	Depressed frontal bilateral	Pneumocephalus and meningitis appeared about a month after injury	Right frontal lobe	Fracture elevated; one dural rent sutured; second rent repaired by muscle and fascia lata graft	Recovery
6	41	M	Occipital and questionable right frontal	Immediate appearance of cerebrospinal rhinorrhea and pneumocephalus	Lateral ventricles and entire subarachnoid space	Not operated; pneumococcus meningitis developed	Death
7	44	M	Extensive comminuted frontal bilateral	Cerebrospinal rhinorrhea developed one week; pneumocephalus seven weeks after injury	Right frontal lobe; lateral ventricles	Explored; dural rent repaired by fascia lata and muscle graft	Recovery
8	19	M	Extensive depressed frontal fracture involving right frontal sinus	Cerebrospinal rhinorrhea and pneumocephalus appeared about three weeks after injury	Right frontal lobe	Elevation of depressed fracture; exploration for pneumocephalus; dural rent repaired by suturing and fasci lata graft	Recovery

no vision in the eye was evident. The right fundus at this time showed an advancing optic atrophy. The retinal hemorrhage was fading. He showed no positive neurologic signs. Roentgen examination of the skull on July 27 showed the comminuted fractures of the frontal bone as before, but in addition a very large pneumocephalus of the right frontal lobe was seen (figs. 16 and 17).

Within a day or two the cerebrospinal rhinorrhea ceased and the headache decreased. Further roentgenograms taken on August 6 showed that the amount of air in the frontal lobe had greatly decreased. The patient was observed for about ten days more. On August 14 he again noticed some fluid coming from the right side of his nose. He sneezed on one occasion and immediately experienced

an increase in his headache. At this time he was conscious of a sizzling sound in the right side of his head, probably when the air rushed in. Further roentgenograms of the skull showed a reestablishment of the original pneumocephalus.

On August 17, a scalp flap was turned back in the right frontal region exposing the fractured area. A fracture line was seen running through the anterior wall of the right frontal sinus, and through this fracture many bubbles of air gushed out. It was not feasible to attempt to turn a bone flap. Two of the larger fragments were removed, permitting retraction of the dura over the tip of the right frontal lobe. This membrane was found to be badly torn, and considerable laceration of the frontal lobe was seen. One was able to demonstrate a fracture line running down the posterior wall of the right frontal sinus. At one point an opening was present which permitted the passage of a probe directly into the sinus. It was impossible to suture the dura. A fascia lata graft was placed over the opening in the posterior wall of the frontal sinus, and muscle grafts covered the rent in the dura. The fragments of bone were replaced, and the wound was closed tightly.

The postoperative course was satisfactory with stoppage of the cerebrospinal fluid leak and disappearance of headache. However, vision in the left eye did not return. The patient left the hospital on September 9 otherwise apparently well.

#### SUMMARY

Eight cases of traumatic pneumocephalus are reported. Three patients of this group died of meningitis, two of them succumbing from pneumococcus and one from streptococcus meningitis. Only one of these three patients was operated on, the operation being performed after meningitis had become general; in this instance, the tear in the dura was not found. Operation was performed in five cases with recovery; in each instance, the opening in the dura was found and closed, either by suture or muscle graft.

Any case of fracture of the skull communicating with an accessory nasal sinus, particularly the frontal, should be closely watched for the possible development of pneumocephalus. This complication may appear at once or more often several weeks after the injury. The presence of cerebrospinal rhinorrhea should increase precautionary measures. The patient should be warned against sneezing, coughing or any action that may intensify the air pressure in the accessory nasal sinuses. If pneumocephalus is demonstrated, whether the air is present in the frontal lobe, lateral ventricles or both, its removal should be attempted at once, together with closure of the dural rent. Signs of meningitis are often present, even in the absence of infecting organisms; consequently, they should not necessarily deter an attempt to correct the pneumocephalus. It may even be justifiable to proceed in certain cases in which infecting organisms have been demonstrated in the fluid. The prognosis in cases of pneumocephalus is probably better if operative rather than expectant treatment is used. Success depends largely on early recognition and prompt intervention.

# EXPERIMENTAL SHOCK

THE CAUSE OF THE LOW BLOOD PRESSURE PRODUCED BY  
MUSCLE INJURY \*

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The low blood pressure with which I am concerned in this paper is that which during and since the recent war has been recognized as 'secondary shock'. In contrast with this is the condition that has been termed 'primary shock' or 'collapse'. A satisfactory explanation for the latter condition seems to have been offered by Goltz<sup>1</sup> in 1863, when he found that a blow on the exposed mesentery of the suspended frog caused reflex inhibition of the heart through the vagus and a lessening of vascular tone generally throughout the body and especially in the abdominal cavity. As regards "secondary shock" many suggestions have been presented to account for the low blood pressure and other phenomena. The older ideas are enumerated in Groeninger's treatise,<sup>2</sup> while the more recent ones are described in detail in Cannon's monograph.<sup>3</sup>

Of the theories that have been advanced as to the cause of "secondary shock," the most divergent views have been expressed by those who maintain that it is associated with a general relaxation of the large vessels and those who maintain that it is accompanied by marked constriction of the arteries. Crile<sup>4</sup> and his associates have been the most arduous proponents of the former theory which stipulates that prolonged sensory stimulation produces exhaustion of the vasomotor center that a fall in the arterial blood pressure accompanies the exhaustion of the vasomotor center and that this produces an accumulation of blood in the large veins. Crile thought that this accumulation of blood in the large veins diminishes the diastolic filling of the heart and hence its output. Mapother<sup>5</sup> and later Malcolm<sup>6</sup> were among the first supporters of the second theory which states that the arterioles are markedly con-

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1 Goltz, Virchow's Arch. i. path. Anat. **26**: 50, 1863; **29**: 394, 1864.

2 Groeninger, Ueber den Shock, Wiesbaden, J. F. Bergmann, 1885.

3 Cannon, Traumatic Shock, New York, D. Appleton & Company, 1923.

4 Crile, An Experimental Research into Surgical Shock, Philadelphia, J. B. Lippincott Company, 1899.

5 Mapother, Brit. M. J. **2**: 1023, 1879.

6 Malcolm, Tr. M. Soc. London **32**: 274, 1900.

stricted in shock. It was believed by Malcolm that this constriction expressed plasma from the blood stream resulting in a diminution in the circulating blood volume. Most of the investigators subsequent to Malcolm have believed that there is a diminution in the circulating blood volume in shock, but there has been a great deal of disagreement as to what is responsible for this decrease. Starling<sup>7</sup> thought that most of the loss of circulating fluid is into the dilated capillaries of skeletal muscle. He explained the dilatation of capillaries by noting that the arterial blood pressure is usually higher during the exciting period which frequently precedes the injury. Most of the muscles usually become relaxed following a severe injury. The hypertonicity of the arteries and the hypotonicity of the muscles result in a slow flow of blood through the muscles and in an accumulation of blood there with a decrease in the circulating blood volume. Erlanger and his associates<sup>8</sup> reduced the volume of the circulating blood by manipulation of the abdominal viscera, by partial occlusion of the thoracic aorta or inferior vena cava, and by the injection of large amounts of epinephrine hydrochloride intravenously. In these experiments, they noted the distention of the capillaries and venules of the intestinal villi with red blood cells, but they stated, "The mechanism of the dilatation of the capillaries and venules has not been included in the scope of this investigation." The British Medical Research Committee in August, 1917, invited a Special Investigation Committee to work on surgical shock and allied conditions. This committee consisted of Bayliss, Bainbridge, Cannon, Richards, Sherrington, Starling, Dale and others. Their observations were published in "Report of Shock Committee, Special Report Series," nos. 25, 26 and 27. The work is summarized in Cannon's monograph.<sup>3</sup> The method which was employed in producing a low blood pressure, in many of the committee's experiments consisted of traumatizing one of the posterior extremities of cats. They maintained that there was not sufficient bleeding into the wounds to account by itself for the reduction in pressure. Section of the cord in the upper lumbar region, in some experiments, showed that the fall in blood pressure was not due to any general effect of the trauma on the circulation, brought about by nervous agencies. It was assumed that the continued fall in pressure following trauma was produced by the absorption of some depressant substance. The effects of histamine and muscle trauma were compared in various experiments, and it was believed that the hypothetical depressant produced by injuring muscles was either histamine or some fairly closely related substance. The laboratory data were carefully correlated with

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7 Starling. *Arch med belges* **71** 369, 1918.

8 Erlanger et al. *Am J Physiol* **49** 90, 151 and 345, 1919, **50** 31, 104, 119, 1919.

the clinical observations. This theory differs from the others, which consider loss of blood volume, vasoconstriction and capillary congestion as the essential disturbances in "secondary shock," in that evidence for the initiating agent is presented. However it has in common with the other theories the fact that no initiating agent has actually been demonstrated.

There are many other theories which have been advanced in explanation of shock each of which has at least a few proponents. Most of these do not emphasize the reduction in the circulating blood which has been definitely demonstrated by Keith<sup>9</sup> and others. These theories include (1) the theory of inhibition (2) the theory of fat embolism, (3) the theories of suprarenal hyperactivity and hypo-activity (4) the theory of acidosis and (5) the theory of acapnia. All of them lack proof.

The experiments which are to be reported here were suggested by some work performed by Blalock and Bradburn<sup>10</sup>. The oxygen content of blood obtained from various veins was determined in shock, which was produced by several methods. It was found that the oxygen content of blood from the portal vein was much higher after a low blood pressure had been produced by trauma to the intestines than after a proportionate decline in pressure obtained by other methods. The oxygen content of blood from the femoral vein of a traumatized leg was high, while that from the opposite extremity was low. These observations together with others suggested but did not prove that a local accumulation of blood occurs in a traumatized area, and they were considered as evidence against the action of a histamine-like substance which produces a general bodily effect.

Trauma to one of the extremities of the experimental animal produces general phenomena that are closely similar to those seen in patients in shock. It has advantages over other methods of producing a fall in blood pressure in that the opposite extremity can be used as a control and in the fact that the inflow and outflow of blood from the part can be controlled as desired. As stated previously, this method was employed by Cannon and Bayliss<sup>11</sup> in their studies on traumatic shock.

The present study was undertaken in order to try to determine whether the low blood pressure produced by trauma to one of the extremities is due to the formation of some substance which exerts a

9 Keith. Report of Shock Committee. Medical Research Committee no 27, March, 1919.

10 Blalock and Bradburn. Blood Distribution in Shock. A Study of the Oxygen Content of the Venous Blood from Different Localities in Shock Produced by Hemorrhage by Histamine and by Trauma. Arch Surg 20:26, 1920.

11 Cannon and Bayliss. Note on Muscle Injury in Relation to Shock. Report of Shock Committee. Medical Research Committee no 26 pp 19-23 March 1919.



general bodily effect or whether it is due simply to hemorrhage locally. As the first approach, the experiments of Cannon and Bayliss were repeated. As sequelae, then experimental procedure has been altered in various ways.

#### METHODS

The experimental animals in all instances were dogs. Sodium-barbital, administered intravenously, was employed as the anesthetic. The amount given was 0.3 Gm per kilogram of body weight. The anesthesia which was produced by this amount of barbital was sufficiently profound to permit of no evidence of pain when severe trauma was instituted. In several control experiments, the effect of barbital alone on the blood pressure was determined, and there was practically no alteration during the first five hours following its administration. In several animals, there was a rapid decline in the blood pressure shortly after the giving of barbital. These experiments were discarded.

The level of the mean blood pressure was used as the criterion of the degree of shock. This was determined by placing in the carotid artery a cannula which was connected to a mercury manometer. The pulse rate and the temperature were also determined frequently. When the room temperature was high or low, electric fans or warming pads were employed, in some instances, maintaining the temperature of the animal at approximately the normal level.

In all experiments in which the effects of trauma were determined, the injury was produced by striking one of the posterior extremities varying numbers of times with a hammer. The bones were not broken, and most of the blows were struck over the thick thigh muscles. This method of producing shock is almost identical with that described by Cannon and Bayliss.

At the conclusion of most of the experiments in which the effects of trauma were studied, the differences in weight of the posterior extremities were determined. It was found that trauma of sufficient severity to cause a low blood pressure produced an extravasation of blood not only into the tissues of the thigh, but also into the loose tissues of the groin and flank. This observation demonstrated the fact that an amputation at the upper part of the thigh would not determine the true difference in weight on the two sides. The site at which the amputations were performed was in the midabdominal region. The terminal aorta and vena cava were divided between ligatures after making a midline abdominal incision extending from the xiphoid process to the symphysis pubis. The symphysis pubis was divided with a saw. This gave ample exposure for the removal of the bladder and the rectum. The iliac vessels on each side were clamped. The lower part of the body was then removed from the upper by making transverse incisions in the midabdominal region at the same levels on the two sides. Transverse division of the spinal column with a saw completed the amputation. The lower part of the body was then divided into two equal halves by sawing longitudinally through the midline of the spinal column. The tail of the animal was then removed. Each of the two parts was placed in a vessel, the clamps were removed, and the weight of each half determined. There was practically no loss of blood during this procedure.

A sample of blood for a determination of the hemoglobin content was obtained before the animal was killed. After the posterior extremities were removed, an incision was made into the leg which had been traumatized, and a sample of the bloody fluid which was present there was obtained for a determination of the hemoglobin content. An attempt was then made to collect all of the blood from

the two posterior parts. Each of these was placed in a large basin. Multiple incisions were made through each and every part was washed thoroughly with saline solution. The percentage of the hemoglobin of the fluid in the two basins was then determined. These figures when divided by the percentage of the hemoglobin of the blood and multiplied by the amount of fluid in the basins gave the amount of blood which was recovered from the two parts. A comparison of the percentage of the hemoglobin of blood from one of the vessels with that of the hemoglobin of blood from the tissues of the traumatized thigh gave an approximate idea as to the relative losses of red cells and plasma from the circulating blood.

The procedures other than those just mentioned varied in the different types of experiments and they will be described in detail along with the individual groups. The order in which these different groups of experiments is presented is the same in most instances as that in which they were performed. This is mentioned in order to show the manner in which one type of experiment suggested another.

#### OBSERVATIONS

*1 The Effects of Trauma to One Leg No Tourniquet Applied*  
*Is one able to produce a fall in blood pressure to a shock level without enough hemorrhage into the traumatized area to account for the decline?*

Eight experiments of this type were performed. Usually, approximately thirty minutes after the barbital was administered, the blood pressure was determined as a control. One of the legs was then traumatized by striking it a variable number of times with a hammer. The blood pressure fell during the initial part of the trauma, but if the trauma was continued for several minutes longer, it would usually rise. The rate of the fall of the blood pressure appeared to be almost directly proportional to the amount of injury which was inflicted. The length of time which elapsed between the initiation of the trauma and the reduction of the blood pressure to a shock level varied in the different experiments from one hour and fifteen minutes to six hours and twenty-eight minutes. Most certainly this interval could have been either shortened or lengthened by increasing or decreasing the severity of the trauma. When the blood pressure reached a level of 80 mm or below there was always an evident increase in the size of the traumatized leg.

The amount of barbital which was given always caused a marked acceleration of the pulse rate. The rate usually declined after about an hour even though the leg had been traumatized, and it reached a high level again when the blood pressure dropped. The temperature of the animal usually remained at approximately the same level throughout the experiment.

The mean blood pressure immediately before the amputation in the various experiments ranged from 9 to 94 mm of mercury. In three of the experiments the mean pressure was 80 mm or above. In all the experiments, the difference in weight of the traumatized and non-traumatized sides indicated enough loss of fluid from the blood stream

to account for the reduction in the blood pressure to a shock level. If it is assumed that 1 liter (1,000 cc) of blood weighs 1 Kg, the difference in the weights of the legs expressed in cubic centimeters of blood varied in the eight experiments from 530 to 960.

The eight animals varied in weight from 10.9 to 15 Kg. When a normal dog is bled 1 per cent of its body weight at hour intervals, the mean blood pressure is reduced to 70 mm of mercury or below after from three to four hours. In all of the present group of experiments, the difference in weight of the two sides amounted to more than 4 per cent of the body weight. The fact that these animals were able to withstand a larger proportionate loss of blood volume when the bleeding was into the tissues of the leg than other animals could tolerate when

TABLE 1—*The Effects of Trauma to One Leg No tourniquet Applied*

Experiment	Weight of Animal Kg	Control Mean Blood Pressure Mm Hg	Time Interval Between Initial Irrum and Amputation	Mean Blood Pressure Immediately Before Amputation Mm Hg	Weight of Traumatized Part Kg	Weight of Nontraumatized Part Kg	Difference in Weight of Traumatized and Nontraumatized Parts, Kg	Hemoglobin of Blood per Cent	Hemoglobin of Fluid from Leg per Cent	Amount of Blood of Traumatized Part Cc	Amount of Blood of Nontraumatized Part Cc	Difference in Amount of Blood of Traumatized and Nontraumatized Parts Cc
1	12.6	137	3 21'	94	2.26	1.67	0.59	90	73	377	18	359
2	13.7	130	4 34'	83	2.36	1.73	0.63	80	49	375	60	315
3	14.0	121	2 41'	56	2.61	1.74	0.87	55	40	327	46	281
4	12.0	130	2 20'	29	2.40	1.44	0.96	80*		635	23	632
5	12.5	139	6 28'	58	2.32	1.79	0.53	80*		228	26	202
6	14.4	150	2 0'	55	2.62	1.94	0.68	80*		557	24	533
7	10.9	137	3 50'	9	1.72	1.18	0.54	60		391	21	367
8	15.0	120	1 1'	80	2.70	1.96	0.74	70		520	49	470

\* Estimate

bled into a receptacle is explained by the fact that the percentage of the hemoglobin of the fluid from the leg was lower than that of the hemoglobin of the blood stream. This indicates a greater proportionate loss of plasma than of red cells. The results of the eight experiments are given in table 1.

The details of one experiment are given in full.

Protocol. Weight of dog, 14 Kg. At 9 a. m., barbital, 4.2 Gm., injected into the external jugular vein. At 9 32, control mean blood pressure, 121 mm of mercury, pulse, 175, temperature, 101.2. From 9 35 to 9 50, trauma to the right posterior extremity with a hammer. At 9 53, blood pressure, 100. At 10, blood pressure, 101, pulse, 156. From 10 09 to 10 17, further trauma to leg. At 10 20, blood pressure, 96, pulse, 154, temperature, 100. At 10 49, blood pressure, 116. From 10 51 to 10 55, further trauma. At 10 56, blood pressure, 100, pulse, 128, temperature, 99.3. At 11 32, blood pressure, 100. From 11 35 to 11 40, further trauma. At 11 45, blood pressure, 78, pulse, 133, temperature, 99.5. At 12 06, blood pressure, 76. At 12 14, blood pressure, 56, pulse, 180. At 12 16, mid-abdominal amputation performed. The weight of each side and the amount of blood recovered from each are given as experiment 3 in table 1.

It is to be noted that in these eight experiments on dogs anesthetized by barbitol the blood pressure was not reduced to a shock level by trauma to the leg without causing the loss of enough of the blood volume locally to account for it

*2 Effects of Trauma to One Leg Which Has a Tourniquet Placed Tightly Around the Upper Part of the Thigh, Femoral Artery Not Included in Tourniquet Is one able to produce shock? If so, is there enough hemorrhage to account for it?*

Two experiments of this type were performed After the animal was well anesthetized by barbitol, the femoral artery was freed in the extreme upper part of the thigh for a distance of several centimeters A strong rubber tube with a small circumference was placed beneath the artery This tube was pulled tightly around the upper part of the thigh and anchored in place by two strong clamps The leg was then traumatized distal to the tourniquet, care being taken to see that the tourniquet did not become dislodged so as to constrict the artery In order to prevent the tourniquet from pressing on the artery, the foot was then tied to the arm of a ring stand, holding the leg upward and perpendicular to the body of the dog

The blood pressure fell to a shock level in these two experiments after less trauma than was usually necessary in the experiments in which no tourniquet was used Amputation and weighing of the posterior extremities showed enough difference in weight to account for the reduction in blood pressure

The details of one experiment are as follows

Protocol Weight of dog, 167 Kg At 8 55 a m, barbitol 51 Gm, injected At 9 20, blood pressure, 155, pulse, 163, temperature, 101.3 At 9 45, blood pressure, 152 At 10 03, tourniquet placed on tightly, artery outside At 10 04, blood pressure, 154 From 10 10 to 10 18, trauma to the leg distal to tourniquet At 10 25, blood pressure, 136 At 10 37, blood pressure, 140, pulse, 180, temperature 102 At 10 55, blood pressure 127 At 11 50, blood pressure, 98 At 12 10, blood pressure, 88, pulse 180 At 12 17, blood pressure, 75 At 12 20, midabdominal amputation performed Weight of traumatized part, 267 Kg, of nontraumatized part, 196 Kg Difference in weight approximately 710 cc of blood or plasma Hemoglobin content of blood from the aorta, 65 per cent, of fluid recovered from traumatized leg 52 per cent Amount of blood recovered from traumatized side, 422 cc, that of blood from nontraumatized side, 34 cc.

These experiments show that shock can be produced in an animal by traumatizing a leg which has a tourniquet around it, the artery being outside, and that there is enough loss of blood volume locally to account for the reduction in the blood pressure

*3 The Effects of Placing a Tourniquet Around the Upper Part of the Thigh, Femoral Artery Outside Tourniquet, No Trauma Is a low blood pressure produced?*

FIVE experiments of this type were performed. After the animal had been given barbital and the control studies had been made the femoral artery was exposed in the upper part of the thigh. The tourniquet was placed around the leg beneath the artery. The blood pressure was determined at approximately half-hour intervals.

The leg distal to the tourniquet became swollen in less than an hour, but never increased in size as much as did the extremities which were traumatized with a tourniquet on. Throughout the course of the observations, the blood pressure declined slightly in two of the experiments, became slightly elevated in two, and remained the same in one. The longest period of observation was four hours and the lowest mean blood pressure recorded, at the termination of the experiments, was 118 mm of mercury.

These experiments show that leaving the femoral artery patent and tightly constricting the upper part of the thigh, without traumatizing the leg, does not result in the production of a low blood pressure.

Since a marked constriction of the upper part of the thigh with the femoral artery patent results in bleeding into the extremity and an increase in its size, but no marked reduction in blood pressure, it was wondered if the bleeding into two posterior extremities similarly prepared would cause a diminution in the blood pressure.

4 *Effects of Placing a Tourniquet Around the Upper Part of Each Posterior Extremity, with Femoral Arteries Outside and No Trauma*  
*Is a low blood pressure produced?*

The procedures were exactly the same as those described for the aforementioned group, except that the two posterior extremities were employed instead of the one. Four experiments of this type were performed. Both legs became noticeably larger within an hour after the tourniquets were applied. The blood pressure declined to a shock level in all experiments. Incisions into the legs at the termination of the experiments showed much hemorrhage into the tissues.

Tourniquets applied tightly to both posterior extremities, the femoral arteries being left outside, cause a reduction in the mean blood pressure to 70 mm of mercury or less.

It has been stated that the application of a tourniquet to one thigh excluding the artery causes little alteration in the blood pressure while a similar procedure on both posterior extremities causes a decline. Histamine is believed to cause an increase in capillary permeability with a loss of fluid from the blood stream. It seemed desirable to determine whether or not the injection of histamine into the excluded femoral artery after a tourniquet had been placed around the thigh would alter the behavior of the blood pressure.

5 *Effects of Injection of Histamine into the Femoral Artery Which Is Outside of a Tourniquet Placed Around the Thigh Segments of Femur Resected* Does the blood pressure behave in the same manner as in a similar procedure without the injection of histamine?

The original idea in this group of experiments was to determine whether it was possible to produce a low blood pressure by injecting histamine into the femoral artery of a thigh which was surrounded by a tourniquet the artery being outside. Previous experiments had shown that a low blood pressure was not produced when histamine was not injected. It was thought that this would give some information as to whether or not a histamine-like substance was responsible for part of the hemorrhage that occurs when a tourniquet circumscribes the structures of the thigh with the exception of the femoral artery.

In the first five experiments of this group histamine was injected into the femoral artery distal to a bull-dog clip which was occluding the artery temporarily. The tourniquet had been placed around the thigh before the histamine was injected. The clip was placed on in order to guard against the back flow of histamine in the femoral artery. The amount of histamine injected in most instances was 10 mg. In three of the five experiments there was an almost immediate decline in the blood pressure as soon as the histamine was injected. In one of the experiments there was a drop in the pressure as soon as the clip was removed from the artery, and in the remaining experiment the blood pressure was not altered by the injection of histamine. It was evident from these experiments that the placing of a tourniquet tightly around the thigh does not rule out the possibility of the absorption of toxic products from the part distal to the constriction. The most likely route for the return of the histamine into the general circulation was thought to be through the vessels of the femur.

In a series of eight experiments approximately 5 cm. of the upper shaft of the femur was removed. The length of bone which was left attached to the head of the femur was about 7 cm. A tourniquet was then placed around the upper part of the thigh the artery being excluded and histamine was injected into the artery distal to a bull-dog clip. There was no marked change in the blood pressure in five of these experiments and there was a definite decline in three. This indicated that there was still in some instances the possibility for the return of blood from the extremity.

In four experiments an incision was made on the lateral surface of the upper part of the thigh over the greater trochanter of the femur. A Gigh saw was placed around the neck of the femur and the neck was divided. Approximately 7 cm. of the upper part of the femur was then removed. This caused little loss of blood. Gauze was packed in

the cavity that resulted from removing part of the femur. The femoral artery was then dissected free in the groin, and a tourniquet was placed tightly around the upper part of the thigh. Histamine varying in amounts from 10 to 26 mg. was injected into the femoral artery distal to a bull-dog clip. No fall in blood pressure resulted. Neither did the removal of the clip from the artery result in any appreciable fall in pressure even when the observations were extended over a long period of time. The fact that the histamine remained in the leg was demonstrated by removing the tourniquet at the end of the experiment and noting the abrupt fall in the pressure. The fact that histamine causes no more fall in pressure when injected under the conditions enumerated than does the simple application of a tourniquet, excluding the artery, is demonstrated by comparing these experiments with those in which histamine was not injected. The results of a single experiment are given in detail.

Protocol. Weight of dog, 14.5 Kg. At 8:50 a. m., barbital, 4.3 Gm., injected. At 9:18, control studies, blood pressure, 116, pulse rate, 180, temperature, 103. At 9:27, blood pressure, 112. From 9:35 to 9:43, neck of femur divided, 7 cm. of upper part of femur removed. At 9:45, blood pressure, 107. At 9:50, tourniquet placed around upper part of thigh, femoral artery outside. At 9:51, blood pressure, 109. At 9:53, femoral artery occluded by a clip, 10 mg. histamine injected distal to the clip. At 9:54, blood pressure, 112. At 9:57, clip removed from femoral artery. At 9:59, blood pressure, 111, pulse, 180, temperature, 103. At 10:05, blood pressure, 110. At 10:30, blood pressure, 120, pulse, 180, temperature, 102.8. At 11, blood pressure, 128, pulse, 180. At 12:15, blood pressure, 123. At 1:20, blood pressure, 110, pulse, 180. At 1:25, tourniquet removed from around thigh. At 1:26, blood pressure, 35. At 1:33, blood pressure, 34.

Such results indicate that the extreme upper part of the femur must be removed in order to be certain that there will be no return of blood from the extremity which has a tourniquet around it. They also indicate that the injection of histamine into an extremity which is surrounded by a tourniquet, the artery being outside, does not alter the behavior of the blood pressure. This last statement is interpreted as meaning that there is as much loss of fluid from the blood stream under these conditions without the injection of histamine as there is with it.

In the previous experiments in which the effects of the application of a tourniquet to one or both legs were determined and also in the experiments in which the effects of trauma after applying a tourniquet were studied, the possibility of the absorption of toxins from the extremity was not eliminated. The repetition of these experiments after removing the upper part of one or both femora appeared to be indicated. The previous experiments were included in this report because the conditions attending their performance more nearly approach

the normal since the removal of part of the femur is associated with a moderate amount of trauma. Next, however, the effects of the simple removal of the upper parts of both femora were determined.

6 *Control Experiments on the Effects of Removal of a Part of the Femur on Each Side. Do the operations alone cause a fall in blood pressure?*

Two experiments of this type were performed. The length of the portion of the femur which was removed in each instance was about 6 cc. In one experiment, the mean arterial pressure was 140 mm of mercury before the femora were resected, and the pressure was 130 mm of mercury seven hours after the operation. In the second experiment the mean arterial pressure was 110 mm immediately preceding the operation and it was 107 mm six and one-half hours later.

These experiments show that parts of the femora of dogs may be removed without causing a fall in blood pressure.

7 *Effects of a Tourniquet on Leg, Artery Outside, After Resection of the Upper Portion of One Femur, No Trauma. Does a fall in blood pressure result?*

The procedure in these experiments was the same as that in group 3, except that part of the femur was removed in the present ones. Four experiments of this type were performed. The duration of the application of the tourniquet varied in the different experiments from two hours and twenty minutes to four hours. There was practically no alteration in the blood pressure, there being a slight rise in two experiments and a slight fall in the remaining two.

In these experiments, as in those in which the femur was not resected, the application of a tourniquet to the thigh, the femoral artery being outside, did not cause a significant alteration in the blood pressure.

In two additional experiments, an amount of blood was allowed to flow from the carotid artery which equaled 1 per cent of the weight of the dog. The structures of the upper part of the thigh with the exception of the femoral artery, were then constricted by a tourniquet. The mean blood pressure in one dog was 67 mm after the tourniquet had been in place for five hours, and the other dog died two and one-half hours after the application of the tourniquet.

8 *Effects of Tourniquets on Both Thighs, Arteries Outside After Resection of the Proximal Portions of Both Femora, No Trauma. Does a fall in blood pressure result?*

The results of the four experiments of this type were the same as those in group 4, in which tourniquets were applied to the thighs without removing parts of the femora on each side. In the first experiment the mean blood pressure was 73 mm of mercury two hours after



the tourniquets had been applied, in the second experiment, the pressure was 22 mm two hours and seven minutes after the application of tourniquets, and in the third and fourth experiments the pressures were 72 and 77 mm of mercury, respectively three hours after the tourniquets were placed around the thighs

These experiments show that the application of tourniquets to both posterior extremities, the femoral arteries being outside results in a marked decline in the blood pressure

*9 Effects of Trauma with Tourniquet on, Artery Outside, after Resection of the Upper Portion of One Femur Does a fall in blood pressure occur? If so, is there sufficient hemorrhage to account for it?*

TABLE 2—*The Effect of Trauma to One Leg, Femur Resected, Tourniquet Applied, Artery Outside*

Experiment	Weight of Annumal, Kg	Time Interval Between Initial Trauma and Amputation	Mean Blood Pressure Immediately Before Amputation Mm Hg	Weight of Traumatized Part Kg	Weight of Nontraumatized Part, Kg	Difference in Weight of Traumatized and Nontraumatized Parts, Kg	Hemoglobin of Blood per Cent	Amount of Blood of Traumatized Part cc	Amount of Blood of Nontraumatized Part, cc	Difference in Amount of Blood of Traumatized and Nontraumatized Parts cc
1	18.2	3 15	84	2 12	2 20	0.08				
2	10.4	2 5	45	2.04	1.61	0.43				
3	9.7	1 48	25	2.68	1.65	0.43	80*	372	10	362
4	16.4	2 12	0 (dead)	2.98	2.23	0.75				

\* Estimate

The procedure in these experiments was the same as that in group 2, except for the removal of the upper part of the femur. Four experiments of this type were performed. There was a definite decline in the blood pressure in all instances, and the difference in weight of the two extremities indicated sufficient loss of blood volume to account for the drop in pressure.

The results of these experiments are tabulated in table 2.

The details of one experiment are as follows:

*Protocol*—Weight of dog 10.4 Kg. At 9 25 am barbitol 3 Gm, injected. At 9 40 control mean arterial pressure 135 mm of mercury, pulse rate, 120, temperature 103.2. At 10 05 left femoral artery exposed, upper part of left femur removed. At 10 06 blood pressure 137. At 10 11, tourniquet placed around upper thigh artery outside. At 10 12, blood pressure 135. From 10 14 to 10 20, trauma to the left leg distal to tourniquet. At 10 22, blood pressure, 150 pulse rate 180 temperature 103. At 11 05, blood pressure, 144. At 11 37 blood pressure, 135. From 11 39 to 11 44 trauma to left leg. At 11 46, blood pressure, 114 pulse rate 185, temperature, 103. At 12 05 blood pressure, 64. At 12 12 blood pressure 52. At 12 13 clip placed on femoral artery, and 12 mg histamine injected distal to clip. At 12 15 blood pressure 47. At 12 16

clip removed from artery. At 12:20 blood pressure 45. At 12:21 amputation performed. The figures for the differences in weight and amount of blood are given in table 2, experiment 2.

These experiments show that a low blood pressure can be produced by traumatizing one leg which is surrounded by a tourniquet, the artery being outside and that the decline in pressure is due to the bleeding into the tissues distal to the tourniquet.

In the succeeding two groups of experiments the effects of the reestablishment of the return circulation from the parts that had been occluded by tourniquets were determined.

10 *Effects of Removal of the Tourniquet from a Thigh the Femoral Artery of Which Had Not Been Occluded* (1) *When No Trauma Had Been Inflicted* and (2) *When the Part Had Been Traumatized*. Does the removal of the tourniquet cause a fall in blood pressure?

These two types of experiments are reported together because their results are almost identical. In some experiments the femur was not resected while in others the upper part was removed. The results were the same whether a part of the femur was or was not removed. Eight experiments were performed. The tourniquet was left in place for periods of time varying from one hour and forty-four minutes to seven hours. The blood pressure declined in all instances on removal of the tourniquet, the greatest immediate fall being 30 mm of mercury and the smallest fall 8 mm. The blood pressure was observed for periods varying from twenty minutes to three hours and forty-seven minutes following the removal of the tourniquet. In four of the experiments it became elevated slightly, and in four experiments it continued to fall slowly.

In two additional experiments, the effects of releasing tourniquets which had been placed around both posterior extremities were determined. The femoral arteries were not included in the tourniquets and the extremities were not traumatized. Removal of the tourniquets resulted in a definite fall in blood pressure in both experiments.

If a tourniquet was again placed around the leg after it had been left off for a while, the blood pressure would usually rise slightly. In one experiment, there was a definite fall in blood pressure following the replacement of the tourniquet.

Release of a tourniquet which had been constricting all of the structures of the upper part of the thigh with the exception of the femoral artery resulted in a fall in the blood pressure. The reason for this was not apparent. One possible explanation was that some toxic substance had been formed in the extremity which when liberated into the general circulation caused a fall in blood pressure. Another possibility, a view which will be analyzed, was that the removal of the

constriction allowed blood to flow into the tissues which had been compressed in the immediate vicinity of the tourniquet. These tissues had necessarily become anoxic, and hyperemia almost certainly occurred when the constriction was released. An added possibility in the experiments in which trauma was produced was the likelihood that further hemorrhage would take place into the tissues which had been previously compressed by the tourniquet. It seemed desirable to have a method by which the blood could be allowed at will to return from the leg without removing the tourniquet. Isolation of the femoral vein in the groin as the femoral artery had been prepared in most experiments afforded this opportunity. The lumina of the femoral artery and vein could then be opened or closed as desired by a bull-dog clip.

11 *After the Femoral Artery and Vein Have Been Dissected Free in the Groin, the Vein Being Occluded by a Clip, and a Tourniquet Placed Around the Thigh Beneath the Two Vessels, a Study of the Effects of (a) Removal of the Clip from the Femoral Vein of One Leg Which Has Not Been Traumatized, (b) Removal of the Clips from the Femoral Veins of Both Posterior Extremities Which Have Not Been Traumatized, and (c) Removal of the Clip from the Femoral Vein of One Leg Which Has Been Traumatized. Does the removal of the clip from the vein cause a decline in the blood pressure?*

(a) The effects of removal of the clip from the femoral vein of a leg which had been constricted by a tourniquet were determined in two experiments. The upper part of the femur was removed before the tourniquet was applied, in one of these experiments, and the femur was left intact in the other. The thigh was constricted by the tourniquet for three hours, in one experiment, and five hours in the other, before the clip was removed from the vein. Removal of the clip from the vein resulted in a temporary rise in the blood pressure. The blood pressure then slowly declined and remained at approximately the level that existed before the clip was removed from the vein.

(b) The effects of removing the clips from the femoral veins of the two posterior extremities which had been constricted by tourniquets were determined in three experiments. The upper parts of the femora were removed in two of these. The results were approximately the same in all experiments. The blood pressure rose about 10 mm of mercury as soon as the clips were removed from the veins. A slow drop in the pressure followed this initial rise, but the decline was no more rapid than that which had been taking place before the clips were removed. The veins were again occluded by clips after varying intervals of time, and no elevation of the blood pressure was observed.

The details of one experiment are as follows

Protocol Weight of dog 17.8 Kg At 8:40 a.m. barbital 5.4 Gm injected into external jugular vein At 9:18 control blood pressure, 105 pulse 120 temperature 102.2 From 9:35 to 10:07 cm of upper end of each femur was removed At 10:03 blood pressure 112 pulse 144, temperature, 101.8 At 10:12 tourniquets applied to both thighs femoral artery and vein not occluded by tourniquet femoral vein occluded by a clip At 10:15 blood pressure, 118, pulse 144 At 11 blood pressure 133, pulse 165 At 12 blood pressure 108 temperature 102.8 At 12:30 blood pressure 94 pulse 180 At 1, blood pressure 80 At 1:14 blood pressure 77 pulse 180, temperature, 103 At 1:15, clips removed from the femoral veins At 1:16, blood pressure, 88 At 1:20, blood pressure 80 At 1:25 blood pressure 76 At 1:30, blood pressure, 73 At 1:42 blood pressure 68 At 2:01 blood pressure 62, pulse 195 At 2:25, blood pressure 54 pulse 185 At 2:46 blood pressure 50 At 2:47, femoral veins occluded by clips At 2:49 blood pressure 47 At 3, blood pressure 49 At 3:15 blood pressure 45 At 3:30 blood pressure, 45 At 3:34 clips removed from veins pulse 190 temperature 103 At 3:35, blood pressure 56 At 3:40 blood pressure 49 At 4 blood pressure 46 At 4:30, blood pressure 44

(c) Eight experiments of this type were performed The procedure in these experiments was as follows The femoral artery and vein were exposed and freed in the groin The upper part of the femur, approximately 7 cc, was removed The femoral vein was then occluded by a bull-dog clip In some of the experiments, the femoral artery was occluded temporarily by a clip A tourniquet was then placed beneath the femoral artery and vein and it was pulled tightly around the upper part of the thigh The leg was then traumatized distal to the tourniquet with a hammer

If the femoral artery, as well as the vein, was occluded by a clip during the traumatization and for a considerable period thereafter, there was no fall in the blood pressure until the occlusion of the artery was released In fact, the blood pressure became elevated in all instances above that observed during the control period When the clip was removed from the artery, the blood pressure declined rapidly at first and later more slowly

After the blood pressure had been reduced by varying amounts as a result of the trauma, the clip was removed from the femoral vein In six of the eight experiments, the behavior of the blood pressure was the same There was an immediate small rise in the pressure as soon as the clip was removed from the vein, and after this there was a slow drop in the pressure This decline in pressure was not so rapid as that which had been taking place before the occlusion of the vein was released In three of the six experiments, the artery and the vein were occluded after the effects of releasing the occlusion of the vein had been determined The blood pressure continued to fall in all of these

The details of one of the six experiments follow

Protocol Weight of dog, 11.7 Kg At 8 50 a m, barbital, 3.6 Kg, injected At 9 05, control blood pressure, 111, pulse, 192, temperature, 101.2 From 9 40 to 9 46, 6 cm of the upper end of the left femur removed At 9 50, blood pressure, 112 At 10, tourniquet on, artery and vein outside, artery and vein occluded by bull-dog clips At 10 02, blood pressure, 111, pulse, 170 From 10 05 to 10 15, trauma to left leg At 10 22, blood pressure, 131, temperature, 99.8, pulse, 180 At 10 24, clip removed from the femoral artery At 10 27, blood pressure, 109 At 10 35, blood pressure, 85, pulse, 180, temperature, 100.8 At 10 42, blood pressure, 85 At 10 52, blood pressure, 90, pulse, 110 At 11 12, blood pressure, 94, pulse, 108, temperature, 101.3 At 11 32, blood pressure, 88, pulse, 115 At 11 50, blood pressure, 80 At 12 10, blood pressure, 68, pulse, 110, temperature, 101.4 At 12 14, blood pressure, 58 At 12 15, clip removed from the femoral vein At 12 16, blood pressure, 64 At 12 20, blood pressure, 66, pulse, 110 At 12 22, blood pressure, 65, pulse, 110, temperature, 101.2 At 12 31, blood pressure, 55 At 12 39, blood pressure, 51, pulse, 170, temperature, 100.7 At 12 45, blood pressure, 52 At 12 47, blood pressure, 52 At 12 48, femoral artery and vein occluded At 12 50, blood pressure, 52 At 12 53, blood pressure, 48, pulse, 180 At 1, blood pressure, 38, pulse, 205, temperature, 100.8 At 1 10, blood pressure, 38 At 1 25, blood pressure, 38 At 1 35, blood pressure, 34 At 1 36, clips removed from artery and vein At 1 39, blood pressure, 38 At 1 51, blood pressure, 32 At 1 52, clips on femoral artery and vein At 1 52½, 10 mg histamine injected into femoral artery distal to the clip At 1 55, blood pressure, 33 At 1 57, blood pressure, 32 At 1 58, clip removed from femoral vein At 1 59, blood pressure, 11 At 2 01, animal dead, a midabdominal amputation performed Weight of traumatized side, 2.01 Kg, of nontraumatized side, 1.50 Kg The difference in weight of the two sides, 0.51 Kg, corresponding to approximately 510 cc of blood Hemoglobin of blood, 62 per cent Amount of blood recovered from traumatized side, 492 cc, of that from nontraumatized side, 35 cc, a difference of 457 cc

This experiment, which is typical of the other six, shows that the reestablishment of the venous return from the traumatized part, at least in these experiments, does not cause an acceleration of the fall in the blood pressure. The fact that the blood pressure did not fall when histamine was injected into the artery when the vein was occluded indicated that the tourniquet was preventing the return of any blood from the part. The fact that the animal died as soon as the clip was removed from the vein after the histamine had been injected, indicated that the vein was still capable of transporting blood from the extremity back into the general circulation. A record of the blood pressures which were obtained in this experiment is given in figure 1.

As stated previously, there was an immediate decline in the blood pressure when the clip was removed from the vein in two of the eight experiments. In one of these, the pressure dropped rather slowly, and the animal lived for more than two hours after the occlusion of the vein was released. In the other experiment, the animal died nine minutes after the clip was removed from the vein. The mean blood

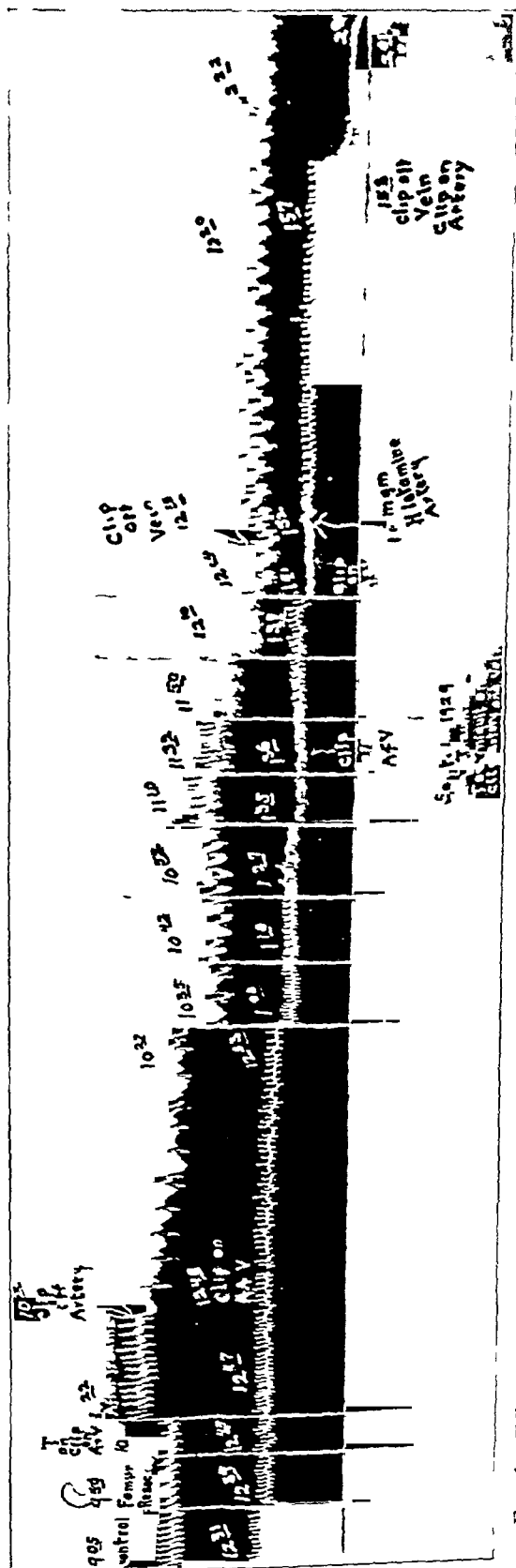


Fig 1—Effects of releasing the occlusion of the femoral vein of a leg which had been tiunitized. The experiment extended from 9 05 a m to 2 01 p m. The numerals indicate the times at which the blood pressure was determined. The curve reads from left to right. I stands for iniquet, A for artery and V for vein.

pressure had been 74 mm of mercury immediately before the vein was released. The reason for the sudden death was not determined. The mean blood pressure had dropped from 144 to 74 mm of mercury during the fifty-four minutes preceding the release of the venous occlusion, but even with such a rapid decline, it is not likely that the sudden death was due to hemorrhage alone. It is possible that sodium citrate was forced into the artery when the arterial cannula was washed out four minutes prior to the termination of the experiment. It is also possible that a toxic substance was formed in the injured area which when liberated into the general circulation caused death.

The great majority of the experiments in this group indicate that the reestablishment of the venous return from an extremity which is constricted in its upper part, except for the artery and vein, does not cause a more rapid decline in blood pressure than would have been expected had the vein remained occluded. The same results were noted in the experiments in which traumatization was an added factor.

*12 The Effects of Occluding the Terminal Aorta and Vena Cava after the Arterial Blood Pressure Has Been Reduced by Traumatization of One Posterior Extremity. What effect has this on the blood pressure?*

The terminal aorta and vena cava were occluded in seven experiments in which the blood pressure had been reduced varying amounts by traumatization of one posterior extremity. The level of the mean arterial pressure just prior to the occlusion varied in the different experiments from 106 to 44 mm of mercury. The blood pressure continued to fall in four of the experiments, became elevated in two, and remained stationary in the other experiment.

Cannon and Bayliss<sup>12</sup> reported the experimental production of a low blood pressure in cats by occlusion of the terminal aorta for one hour. The repetition of this experiment on dogs was the next step undertaken.

*13 The Effects of Occlusion of the Terminal Aorta for One Hour. Is a low blood pressure produced by releasing the occlusion?*

The terminal abdominal aorta was occluded for one hour by a ligature and a bull-dog clip in each of three experiments. During the period of occlusion, the blood pressure either rose slightly above that observed during the control period or remained approximately the same. In one experiment, following the release of the occlusion of the aorta, the blood pressure remained at approximately the same level as that observed during the control period, in one it was slightly higher, and in the remaining experiment it was slightly lower.

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12 Cannon and Bayliss (footnote 11, page 21)

The details of one experiment are as follows:

Protocol Weight of dog 9.1 kg At 8:50 a m. barbital 2.9 gm  
 At 9:31 control mean blood pressure 118 At 9:37 the terminal aorta  
 At 9:38 blood pressure 133 At 10:50 blood pressure, 145 At 10:48  
 pressure 145 At 10:46 occlusion of the aorta released At 10:50, blood pressure 129  
 At 10:57 blood pressure 116 At 11:10 blood pressure, 116 At  
 11:30 blood pressure 116 At 11:42 blood pressure 115 At 12 blood  
 pressure 122

In three experiments the effects on the blood pressure of occlusion of the terminal inferior vena cava for an hour were determined. The alteration in blood pressure which accompanied this procedure was less than that which attended the closing and opening of the aorta.

Occlusion of the terminal abdominal aorta or inferior vena cava of the dog for an hour did not result in the production of a low blood pressure.

Cannon and Bayliss<sup>13</sup> found that massage of a damaged muscle results in a further fall in the blood pressure. This experiment was repeated and supplemented in the next group of observations.

14 *The Effects of Massage of the Traumatized and Nontraumatized Legs* What effect does massage have on the level of the blood pressure?

The effects of massaging the leg which had been traumatized and of massaging the opposite extremity which had not been traumatized were determined many times in several experiments. In almost all instances massaging either extremity caused a fleeting reduction in the blood pressure. The greater decline in pressure resulted from massage of the extremity which had been traumatized. When the nontraumatized extremity was massaged first it caused almost as great a decline in pressure as did massage one minute later of the traumatized extremity. When the traumatized extremity was massaged first, the decline in the pressure was definitely greater than that which resulted from subsequent massage of the leg which had not been traumatized. The figures for the decline in pressure expressed in millimeters of mercury throughout the course of one experiment are as follows: Nontraumatized 15, traumatized 18, traumatized 22, nontraumatized 15, nontraumatized 24, traumatized 28, traumatized 30, nontraumatized 13, nontraumatized 14, traumatized 16. A record of the blood pressure which shows the effects of massage is presented in figure 2.

In two additional experiments, the upper part of one femur was removed, and a tourniquet was placed around the upper part of the thigh. The femoral artery was not included in the tourniquet. No trauma was instituted. After more than an hour, first one extremity

13 Cannon and Bayliss (footnote 11 page 22)



and then the other was massaged. In one experiment, massage of either of the posterior extremities caused a reduction in the blood pressure. The decline was slightly greater on the side that was not occluded by a tourniquet. In the other experiment, there was no definite reduction in the pressure which was caused by massage of either extremity.

These experiments show that massage of either the traumatized or the nontraumatized extremity usually causes a temporary reduction in

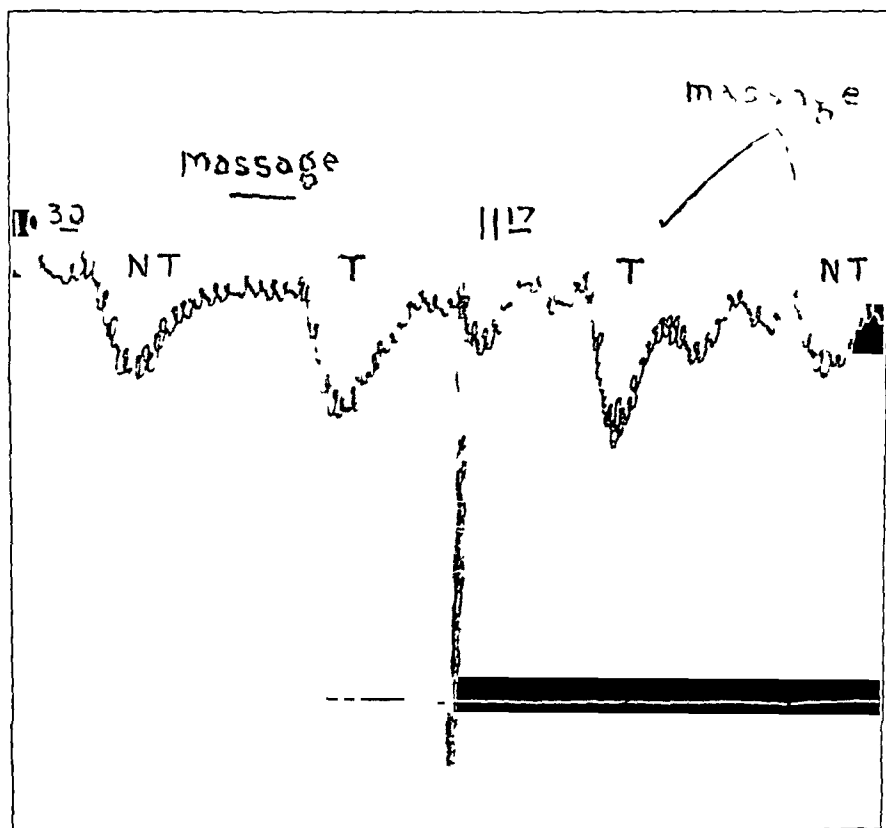


Fig 2—Effects of massage of the traumatized and nontraumatized extremities. The curve reads from left to right. T stands for the traumatized extremity and NT for the nontraumatized one.

the blood pressure, the greater decline occurring after massage of the traumatized side.

An attempt was next made to obtain further evidence of the presence or absence of a depressor substance by transfusion experiments.

15 *The Effects of the Injection of Blood from Dogs in Which the Blood Pressure Had Been Lowered by Trauma to an Extremity into (a) a Normal Dog (b) a Dog in Which the Blood Pressure Had Been Lowered by Hemorrhage and (c) a Dog in Which the Blood Pressure*

*Had Been Reduced by Trauma to an Extent by Which the Blood Pressure*

(a) The donor in this instance had had one leg traumatized to a moderate degree at infrequent intervals during the twenty-four hours preceding the transfusion. The blood pressure at the time was 45 mm of mercury systolic and 32 mm diastolic. All of the blood which was obtainable was taken from this dog and defibrinated. The total amount was 325 cc. At 3:30 p. m. the blood pressure of the recipient was 120 systolic and 85 mm diastolic. At 3:32 transfusion into the external jugular vein was begun. At 3:34 200 cc of blood had been injected and the blood pressure of the recipient was 144/100. At 3:36 with transfusion completed the blood pressure was 140/110 at 3:41 118/75 at 4:00 115/76 and at 4:30 130/80.

(b) The donor in this experiment had had the blood pressure reduced to 75 mm of mercury systolic and 67 mm diastolic by trauma to one extremity. Approximately 200 cc of blood was obtained from this dog and following the injection of saline solution, an additional 300 cc of blood was withdrawn. The blood was defibrinated and kept warm. The recipient weighed 10.5 Kg. At 4:30 p. m. barbitol 3.5 Gm, was given. At 5:30 the control blood pressure was 150 mm of mercury systolic and 110 mm, diastolic. From 5:30 to 5:33 the animal was bled 300 cc. At 5:34, the blood pressure was 25 mm, systolic and 20 mm, diastolic. From 5:35 to 5:38 500 cc of blood which had been obtained from the traumatized dog was allowed to run into the external jugular vein of the recipient. At 5:38 the blood pressure was 170/150 at 5:45, it was 120/86, at 5:55, 130/90 at 6:03, 140/90 at 8:40 14 hours later 144/100.

(c) A low blood pressure was produced in two dogs by trauma to the posterior extremities. The dogs each weighed 8 Kg. At 12:28 p. m., the mean blood pressure of dog A was 50 mm of mercury and that of dog B was 51 mm. At 12:29, the proximal end of the carotid artery of dog B was connected to the proximal end of the external jugular vein of dog A. At 12:31, the blood pressure of dog A was 90. At 12:34, dog B died. At 12:34, the blood pressure of dog A was 93. At 12:37, the blood pressure of dog A was 88. At 12:55 the blood pressure of dog A was 72. At 1:17, the blood pressure of dog A was 67. The experiment was discontinued. Dog B died shortly after its artery was connected to the vein of dog A, and it is likely that the amount of blood that passed from B to A was not great.

No evidence for the existence of a depressor substance in the blood of a dog in which the blood pressure had been reduced by traumatization was found in these transfusion experiments.

16 *The Effects on the Macroscopic and Microscopic Appearance of the Gallbladder of (1) the Intravenous Injection of Histamine, and (2) Trauma to an Extremity Is an alteration in the appearance of the gallbladder produced by either one or both of these procedures?*

Bradburn and Blalock<sup>14</sup> found that the intravenous injection of histamine in amounts sufficient to produce a sustained lowering of the blood pressure causes changes in the gallbladder. The usual bluish appearance of the gallbladder is lost and it assumes a whitish color. The walls of the gallbladder become thickened, the gallbladder decreases in size and contains less bile. Microscopic examination shows a great deal of edema. No alteration in the appearance of the gallbladder was produced in any of the experiments reported here, except those in which histamine was injected.

Injection of histamine causes alterations in the gallbladder. Trauma to an extremity produces no such change.

#### COMMENT

"A primary consideration in the experimental study of natural phenomena is that the reproduction of the phenomena under controllable conditions shall resemble as closely as possible the occurrences in nature." This statement quoted from Cannon<sup>15</sup> expresses the opinion held by Cannon and Bayliss<sup>12</sup> to the effect that the circumstances which attend the experimental production of shock by trauma to extremities are more closely comparable with those in some cases of shock in man than those when a low blood pressure is produced by other methods. It is certain that no operation on the intestinal tract of the human being is associated with as much trauma as is necessary for the experimental production of a low blood pressure by intestinal manipulation. It is extremely difficult to produce shock experimentally by injury to the central or peripheral nervous system. A low blood pressure is comparatively easily produced experimentally in animals by traumatizing large areas of muscle. This method lends itself to controllable conditions more readily than any other. The method is objectionable as are all means in which gross injury of tissue is produced, in that the experiments must be performed on animals that are continually anesthetized or on decerebrate animals.

Many comparisons will be made in this discussion between the results reported here and those obtained by the "Shock Committee," Cannon and Bayliss, in particular. Attention will be focused largely on the "toxemia theory of shock," because most of the recent experi-

<sup>14</sup> Bradburn and Blalock. Unpublished results on the effect of histamine upon the gallbladder.

<sup>15</sup> Cannon (footnote 3 page 142)

mental work has supported it and because my personal undertaking this work was that it offered the most satisfactory explanation for the initiation of events leading to the production of a blood pressure and the associated observations. This opinion is not supported by the experimental work herein reported.

The experiments of Cannon and Bayliss<sup>11</sup> were performed on cats anesthetized by ethyl carbamate (urethane). An iron block was placed at one side of the thigh and the flexor group of muscles was struck six or seven times with a hammer, "so that they were ruptured and severely bruised." In most instances, the skin was not broken and the femur was not fractured. Regarding the condition which was produced by the traumatization, they stated "As time passed after the traumatization, the muscles underwent much swelling, and at autopsy there we found varying amounts of extravasated blood. In no case, however, was there sufficient bleeding into the wounds to account, by itself alone for the effects observed." The amount of bleeding into the injured extremity was determined by Cannon and Bayliss by removing the two hind limbs by symmetrical cuts and weighing them. In the experiments which were performed at a later date by Cannon,<sup>12</sup> dogs and rabbits as well as cats were used. Ether was employed as the anesthetic in these experiments and the amount of ether which was used was reduced after the blood pressure had reached a fairly low level. Cannon stated, "The development of the low blood pressure after tissue injury was proved not to be due to loss of fluid from the systemic circulation, by carefully skinning the posterior extremities after death, disarticulating the legs at the knee and removing the thighs at the hip by symmetrical cuts through the tissues, the thighs were then weighed." He found that the difference in weight of the two sides was as low as 11 per cent of the estimated weight of the blood of the animal.

The results of the experiments reported here are seemingly contrary to those of Cannon and Bayliss<sup>11</sup>. The reason for this discrepancy is not apparent, as the methods which were employed in producing the decline in blood pressure are almost identical. The most likely explanation for the discrepancy is believed to be that it is due to the difference in the methods which were employed in the determination of the weights of the traumatized and nontraumatized parts. The two extremities were amputated by Cannon and Bayliss by symmetrical cuts across the thighs. There are several objections to this method. It is impossible to be sure that the level of the amputation is the same on the two sides because of the thick layers of muscle there and because of the irregular contour of the thigh. After a thigh has been traumatized severely, it is not

<sup>11</sup> Cannon. Some Characteristics of Shock Induced by Tissue Injury. Report of Shock Committee Medical Research Committee no. 26 p. 27. March 1910.

possible to cut across it without the loss of some blood. Trauma to a thigh results in some bleeding into the loose tissues of the groin and flank, and this blood is not included in the amputated part when the incision is made across the upper part of the thigh. These objections were overcome in the present experiments by performing the amputation in the midabdominal region after ligation of the abdominal aorta and vena cava and clamping of the iliac vessels on both sides. In control experiments in which no trauma was instituted, the weights of the two parts were practically identical. The difference in weight of the parts in all experiments in which a low blood pressure was produced by trauma to one extremity amounted to at least 4 per cent of the body weight or almost half of the calculated blood volume. The level of the mean arterial pressure at the time of amputation in three experiments was 80 mm. of mercury or above, which indicates that hemorrhage initiates and is not one of the subsequent events in the declining blood pressure.

In some of the experiments of Cannon and Bayliss,<sup>17</sup> the spinal cord was transected above the lumbar plexus so that all the nerves to the leg which was to be injured were severed. Trauma to the denervated extremity then resulted in changes similar to those obtained in experiments in which the nerve supply was intact. Cannon and Bayliss stated, "The chief interest of the results obtained lies in the demonstration that they are not due to nervous reflexes but to the absorption of some toxic substances given off by the injured tissues." It did not seem necessary to repeat these observations in the present experiments because hemorrhage was sufficient to account for the reduction in blood pressure in the presence of an intact nerve supply and it most certainly would have been sufficient in a denervated extremity.

The experiments which were performed by Cannon and Bayliss were later repeated by Bayliss.<sup>17</sup> He found that a low blood pressure could not always be produced in strong healthy cats by traumatization of an extremity. He removed 15 per cent of the blood volume of cats in which the blood pressure had been reduced by traumatization, but in which a spontaneous recovery was apparently taking place. The blood pressure was lowered greatly by the loss of blood, and he stated, "The loss of this amount of blood is rapidly recovered from by the uninjured cat." However, this is not proof of the presence of a depressor substance, since bleeding a dog of 15 per cent of its blood volume produces a low blood pressure, provided there has been a considerable amount of blood lost previously. This was demonstrated in some of the experiments reported here. The tight application of a tourniquet to the

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<sup>17</sup> Bayliss. Further Observations on the Results of Muscle Injury and Their Treatment. Report of Shock Committee. Medical Research Committee, no. 26 pp. 23-26, March, 1919.

upper portion of the thigh after the upper part of the femur has been removed and the femoral artery has been placed outside the capsule. This operation causes little alteration in the level of the blood pressure. It bears out the fact that when the tourniquet is applied blood is removed from the animal which amounts to 1 per cent of its body weight or approximately 15 per cent of its blood volume. The blood pressure usually falls to a low level after the tourniquet has been in place for a long while. This decline in blood pressure takes place without any gross trauma and without the possibility for the return of any depressant substance from the extremity. The absence of any return of blood from the extremity was demonstrated when the injection of histamine into the femoral artery produced no alteration in the blood pressure. A similar fall in blood pressure was obtained without inducing external hemorrhage by constriction of both thighs by tourniquets by the method described. Here again there was neither trauma nor possibility of the return of depressant substances from the extremities. A low blood pressure was produced by traumatization of an extremity distal to a tourniquet which constricted all the structures of the upper part of the thigh except the femoral artery. The upper part of the femur was removed in most of these experiments and the injection of histamine indicated that there was no return of blood from the part. Amputation and weighing of the extremities showed that there was enough loss of fluid from the blood stream into the traumatized leg to account for the reduction in the blood pressure.

Cannon<sup>16</sup> found that the blood pressure failed to fall at the usual time following muscle injury if the blood vessels to the injured area were tied. These observations were confirmed in the present experiments. In one of these, the thigh was constricted by a tourniquet and the femoral artery and vein were occluded by clips for almost five hours following the initiation of the trauma. The blood pressure was higher at the end of this period than it had been before the leg was traumatized. In one of Cannon's experiments the occlusion of the vessels was released thirty-three minutes after the traumatization and a fall in blood pressure resulted. He stated 'The experiment just mentioned (fig. 2) indicated that some substance given off from the injured tissue was the cause of the drop in pressure for the permanent fall occurred only where the blood was permitted to flow in and out of the damaged region thirty-three minutes after the traumatism. The present experiments have indicated that it is not necessary to have the blood flowing out of the damaged region in order to obtain a decline in the blood pressure. The presence of a patent femoral artery which allows the hemorrhage to take place is all that is necessary. The experiment reported by Cannon in which the occlusion of the arteries and veins was released did not indicate necessarily that the decline in pressure was due to some depressant substance given off by the injured

tissue, for hemorrhage occurs after trauma in the presence of a patent artery regardless of whether the veins are or are not occluded. In further experiments, Cannon<sup>10</sup> ligated the blood vessels of an extremity after a low blood pressure had been produced by traumatization. He found that the blood pressure might begin to rise after the vessels were ligated and that the pressure, in some instances, reached the level which existed before the trauma. It is known that hemorrhages of moderate severity are followed by a dilution of the blood in an attempt to restore the blood volume to the previous level. In the experiments in group 12, described in this paper, the terminal aorta and vena cava were ligated after the blood pressure had been reduced varying amounts by trauma to an extremity. The effects of this procedure were variable, in some instances there was a continued decline and in others a rise in the blood pressure. The impression was gained that the behavior of the blood pressure depended on whether or not a dilution of the remaining blood volume took place. If the decline in the blood pressure were due entirely to the action of some toxin, then the blood pressure would probably rise in all instances when the pathway for the return of this toxin into the general circulation was occluded, provided that the pressure had not been reduced to a low level for a long period of time. Evidence for this was not obtained in the present experiments. As regards the spontaneous rise in the blood pressure which may occur after small amounts of trauma, Cannon stated, "If the tissue damage has not been too great, the pressure may fall to less than 100 mm of mercury, and then spontaneously rise to the former level. This result seems to indicate that the toxic material is limited by the amount of injury, and that after it has produced its depressant effect the pressure rises because no more of the material is being produced." The present work indicates that the following would constitute a more likely explanation. Trauma of sufficient severity to the anesthetized dog to cause a decline in blood pressure produces an extravasation of blood and fluid into the injured tissues. The amount of hemorrhage is controlled by the amount of the injury which is inflicted. The rapid loss of part of the circulating blood volume causes a reduction in the blood pressure. The blood volume increases owing to dilution of the blood after the hemorrhage has stopped, provided that the blood pressure has not reached too low a level. The increase in blood volume results in an increase in the blood pressure.

Cannon and Bayliss<sup>11</sup> found that a marked reduction in the blood pressure occurred when a clip which had been occluding the terminal abdominal aorta for an hour was removed. In the one experiment which they report, the terminal aorta of a cat under urethane anesthesia was occluded for sixty-two minutes. The average blood pressure dropped

to 65 mm shortly after the clip was removed. After twenty minutes it had risen to 82 mm and it remained at this level for forty-five minutes. They stated "This experiment shows that the material swept out of a muscular portion of the body by the returning blood contains various metabolites which lower the blood pressure." With a procedure similar to theirs three experiments were performed on dogs and the results are reported in the paragraphs dealing with group 13. The aorta was occluded for the same length of time. The difference in the two procedures is that the experiment reported by Cannon and Bayliss was performed on a cat anesthetized by ethyl carbamate while the experiments reported here were performed on dogs anesthetized with barbital. The results were different. The blood pressure rose above the level observed during the control period when the aorta was occluded. Following the release of the occlusion, the blood pressure assumed a level which was approximately the same as that observed during the control period. These experiments present no evidence for the formation of a toxic material as a result of the temporary suppression of the blood supply. The small alterations in the blood pressure on release of the occlusion may be due to a dilatation of the vessels of the posterior extremities as a result of the local lack of oxygen that had been present.

It was found in the experiments in group 10 that the removal of a tourniquet which had been occluding all of the structures of the upper part of the thigh except the femoral artery resulted in at least a temporary reduction in the blood pressure. This alteration in the pressure occurred whether the leg had or had not been traumatized. It was believed that the most likely explanation for the decline in pressure was either that it was due to the passage of some depressant substance from the traumatized part into the general circulation or that it was due to the filling up with blood of the vessels which had been compressed in the immediate neighborhood of the tourniquet. Even though a narrow tourniquet was used, its application around the thickest part of the thigh rendered a rather large mass of muscle practically bloodless. It would seem that the amount of blood which would return from the femoral vein of the leg in which stasis had been produced would more than compensate for the return of blood to the part which had been rendered anemic. It was thought that information could be gained as to whether the decline in pressure was due to the absorption of some toxic substance or to a local alteration in the circulation by changing the experimental procedure so that the femoral vein could be occluded or opened as desired and the tourniquet could be left in place. This was done by placing the femoral vein as well as the femoral artery outside the tourniquet. Release of the occlusion of the femoral vein after the



tourniquet had been in place for varying periods of time resulted in a temporary rise in the blood pressure in six of the eight experiments. After this initial rise, the blood pressure declined no more rapidly than before the clip was removed from the vein. The patency of the vein was demonstrated by the injection of histamine into the femoral artery at the termination of the experiment. It is believed that the decline in blood pressure which followed the removal of the tourniquet was not due to the action of some depressant substance, because if it were, a similar result should have followed reestablishment of the circulation through the femoral vein of a leg which was occluded by a tourniquet.

Cannon and Bayliss<sup>11</sup> found that massage of muscles which had been injured caused a further fall of the blood pressure. They state, "In connection with the facts given above, it is of interest to note that massage of damaged muscles, unless a nerve happens to be pinched, results in a further fall of blood pressure. The phenomenon has probably some significance in relation to the increase of shock produced in cases of fracture of the femur when the limb is not adequately supported during transit to the casualty cleaning station." It was found in the present experiments that massage of a traumatized extremity usually causes a fall in blood pressure, but the decline is only a momentary one and a drop is obtained by massage of the opposite normal extremity. The decline is usually greater when the traumatized part is massaged. The fact that the pressure declines temporarily when either extremity is massaged is believed to indicate that the massage in some way alters the caliber of the vessels locally with a resultant change in the arterial pressure. The movement of a broken femur may in some ways simulate manual massage of traumatized tissues. However, it seems more likely that the deleterious effects are due to further bleeding caused by injury to the soft tissues near the sharp bone fragments.

The transfusion experiments which are reported here corroborate the observations of Smith,<sup>18</sup> who performed similar experiments. He ligated the femoral artery and vein of one leg and then traumatized it. One hour and fifteen minutes after the traumatism, the clip was removed from the femoral artery and 25 cc. of blood was withdrawn from a branch of the distal end of the clamped vein. The blood pressure fell 20 mm. of mercury. The blood was then injected into the femoral vein of the opposite side, and the blood pressure rose to the original level. In another experiment, blood was obtained from a femoral vein of a traumatized extremity and injected into the femoral vein of a dog which had been bled 15 per cent of the calculated blood volume. He stated, "The transfused blood failed to produce any appreciable effect in

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18 Smith M I. Studies on Experimental Shock with Especial Reference to Its Treatment. *J Pharmacol & Exper Therap* **32** 465, 1927-1928

the recipient ' Neither the experiments of Smith nor those which are reported in this paper prove that a depressant substance is not present in small amounts in the blood obtained from the traumatized part. The effects due to increasing the blood volume of the recipient may overbalance the action of a depressant substance, if such is present. However, neither do they present evidence that a toxin is present.

McIver and Haggart<sup>19</sup> performed cross-circulation experiments in an effort to determine if trauma to muscles gives rise to a substance that lowers the blood pressure. The posterior extremities of one cat were traumatized after ligation of its abdominal aorta and vena cava. A mid-abdominal amputation was then performed on this animal and the distal parts of the abdominal aorta and vena cava were connected to the proximal aorta and vena cava of a cat with a normal blood pressure. The blood pressure of the latter animal in most experiments declined to a shock level within thirty minutes. No conclusions can be drawn from these experiments because the aorta and vena cava of the first cat were ligated before the trauma was instituted. This allowed the second cat to bleed into the traumatized extremities of the first one after the anastomoses were made. An effort was made to repeat these experiments, the extremities being traumatized before ligation of the aorta and vena cava. The attempts failed because of clots that formed in the cannulas connecting the venae cavae.

Many statements are found in the reports by physiologists and clinicians published during and immediately after the war concerning the importance of differentiating between "shock" and "hemorrhage." As regards the observations in "shock," Cannon, Fraser and Hooper<sup>20</sup> stated, "In cases of shock as seen at a casualty clearing station in conditions of warfare the red count of blood taken from various capillaries is higher than that of blood taken from a vein. The discrepancy is greater, the more profound the shock and not infrequently is as much as two million corpuscles per cubic millimeter. Since the venous count is approximately normal, the condition is due to a stagnation of corpuscles in the capillaries. The observations by means of blood counting have been confirmed by hematocrit and hemoglobin determinations." In regard to "hemorrhage" they stated "After hemorrhage and in cases of shock complicated with hemorrhage the hemoglobin reading is relatively low compared with the red count. It is undoubtedly true that hemorrhage outside the body in moderate amounts results in a dilution of the blood. The experiments in group I which are reported in this

<sup>19</sup> McIver M. A. and Haggart W. W. Traumatic Shock. Some Experimental Work on Crossed Circulation. *Surge Gynec. Obs.* **36**: 542, 1923.

<sup>20</sup> Cannon, Fraser and Hooper. Some Alterations in the Distribution and Character of the Blood. Report of the Committee Medical Research Committee no. 25, p. 84, December, 1917.

paper indicate that the reduction in the blood pressure following traumatism to an extremity can be accounted for entirely by the local loss of blood and fluid from the blood stream. In the several experiments in which determinations were made, the reduction in pressure was associated with an increase in both the number of red blood cells and the percentage of hemoglobin. Hence, there may be two types of hemorrhage, that outside the body associated with a dilution of the blood and that into the tissues of the body associated with a concentration. It is well known that the dilution of the blood which occurs after hemorrhage in moderate amounts outside the body is due to the replacement of part or all of the blood volume by the passage of fluid from the tissues into the blood stream. Determination of the percentage of the hemoglobin of the bloody fluid which was found in pools in the injured muscular tissue showed its value to be definitely lower than that of blood obtained from one of the large vessels elsewhere in the body. This probably means that there is a greater proportionate loss of plasma than of red cells after trauma to an extremity. Efforts were made at the completion of some of the experiments to obtain all of the blood from both the traumatized and the nontraumatized extremities. This was impossible. Hence, an accurate determination could not be gained from the results of the experiments of group 1 as to how much of the difference in weight of the two extremities was due to loss of whole blood and as to how much was due to loss of plasma. The fact that the difference in weight of the two sides indicated the loss of fluid from the blood stream which amounted to more than 4 per cent of the body weight in all experiments does not indicate that there is general capillary dilatation elsewhere in the body with pooling of blood. The intestines were examined in many experiments, and no congestion was apparent. There was no free fluid in the peritoneal cavity. The surprisingly small amount of blood which was obtained from the opposite nontraumatized extremity indicated that there was no pooling of blood there. It is believed that these experiments indicate that determinations of the number of red cells and of the amount of hemoglobin do not show whether there has or has not been hemorrhage, but rather whether the hemorrhage is outside the body or into its tissues.

The theory that shock following trauma is due to a toxin was suggested following observations on patients before most of the experimental work was undertaken. Quenu was among the first to stress the possibility that a toxic factor was an important one. A summary of the ideas which had been gained by various men from clinical experience was published by him in 1918<sup>21</sup>. The character of the wounds

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21 Quenu *Rev. de chir.* 56 204 1918

which were seen most commonly during the war was described by Wallace and Fraser<sup>22</sup> as follows

The tissues of the wound are crushed and lacerated and there are widespread contusion and effusion of blood into the surrounding parts. The neighboring blood vessels are often pulped and thrombosed, and as a result of the interference with the blood supply, whole areas of tissue may afterward die and slough away. In these wounds, muscle appears to be affected more than any other tissue; it becomes a mass of dark brown crushed matter without any evidence of striation or vitality. One cannot fail to be impressed by the enormous destruction which even a small fragment of shell will produce, a degree of destruction which is apparently quite out of keeping with size of the fragment, the exaggerated damage depends upon the enormous velocity at which the fragments are traveling.

McNee, Sladden and McCartney<sup>23</sup> commented on the frequency with which extensive injury of muscle tissue was present in the severe and fatal cases. They reported six cases in all of which there were extensive lacerations of muscles without injury to bones or to any vital structure or organ. All ended fatally with the exception of one case. Because of the fact that most of the experimental evidence for the presence of a toxemia following injury to muscles was derived from the experiments of Cannon and Bayliss,<sup>24</sup> it seems justifiable to quote their observations and comments on clinical cases at length. They stated

The nature of the wounds typically seen in cases of wound shock may be judged from the following records made by one of us at a casualty clearing station where only the most severely wounded men were admitted. Some of them were seen by both of us. In reading these records it should be understood that the wounds were often made by large jagged pieces of shell moving at high velocity. When such a missile breaks the humerus or the femur, or the ilium it smashes and tears extensively the overlying muscles, which, in the thigh and hip, form a thick layer. In all the cases there was shock accompanied by acidosis.

In all twelve cases were reported by Cannon and Bayliss. Their description of the injuries is as follows:

E. G. Compound fracture of left ulna and radius, arm nearly severed, wounds of right arm and left side, abdomen opened, intestine and omentum protruding.

C. P. H. Shell wounds of right thigh with fracture of the femur, and of left arm with fracture of the humerus, wounds of the face.

G. D. Wounds of the left arm with fracture, left leg with fracture, flesh wounds of the right thigh and abdomen.

G. I. H. H. Shell wounds of right ankle, of left leg with fracture, and of the muscles of the buttock.

<sup>22</sup> Wallace and Fraser. *Surgery at a Casualty Clearing Station*. London, 1918, p. 31, quoted by Cannon.

<sup>23</sup> McNee, Sladden and McCartney. *Observations on Wound Shock, Especially with Regard to Damage to Muscle*. Report of Shock Committee, Medical Research Committee, no. 20, pp. 33-35, March, 1916.

H J H Bursting shell broke right femur, left tibia and fibula, and injured right arm

A J R Extensive wounds of both legs, left foot and left arm

W G Wounds of buttock with fracture of ilium, also wounds of right foot

P K Fracture of left femur (much comminuted) and right tibia

W A T Wounds of buttock and perineum, muscles below the buttock torn across and smashed in both legs

G K Wounds of both arms, left thigh, left foot, compound fracture of the right thigh

R C Compound fracture of right femur, multiple shell wounds of left femur, buttock and chest

A H Multiple shell wounds, large wound of left loin involving the gluteal muscles, fracture of pelvis, extensive wounds of right calf muscles and the muscles of the left thigh and left calf, and numerous wounds in back and chest

The comment of Cannon and Bayliss on these cases of injury is as follows

It is obvious that with such wounds as these large amounts of muscle would be torn and smashed. And, just as in the animal experiments recorded above, the injured muscle would produce metabolites, which, on being absorbed into the blood stream, would indicate their presence by a decrease in blood pressure, with other signs of shock

One cannot help but be impressed by the multiplicity and the severity of the wounds in these cases reported by Cannon and Bayliss. Perhaps it is true that the injured muscle would produce metabolites which would lower the blood pressure. It is almost certainly true that the amount of hemorrhage which is necessarily associated with such gross injuries would cause some reduction in the blood pressure.

In the great majority of the reports of injured soldiers in which a low blood pressure and other signs of shock were produced, lesions are described, the nature and extent of which were similar to those described by Cannon and Bayliss. However, usually each series of cases includes one or two instances in which death resulted after varying intervals of time and in which no hemorrhage into the tissues was found. It might be added also that in these cases there were no large masses of lacerated muscle. A report of two such patients was made by Wallace<sup>24</sup> as follows

One was buried by the explosion of a shell in a cellar, the other was blown up by a buried shell over which he had lighted a fire. Both exhibited all the classic symptoms of shock, which lasted over forty-eight hours, in both treatment was of no avail. In neither did the postmortem examination show any gross lesion.

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<sup>24</sup> Wallace. Report of Shock Committee, Medical Research Committee, no 26, p 7, March, 1919

There was a great deal of hemorrhage in most of the cases observed by Keith<sup>25</sup>. He described one exception as follows:

Even without hemorrhage shock may be accompanied by a fall of blood volume. This fact was well brought out in a soldier suffering from very severe symptoms of wound shock, who later died. In this case some 24 hours after 600 cc of gum acacia solution had been injected intravenously, the hemoglobin amounted to 125 per cent. At autopsy no definite external wounds were found except a few superficial bruises, and no gross internal hemorrhage had occurred. In this case the blood volume was not directly determined, but the high hemoglobin percentage, particularly after the injection of the gum solution, indicated a reduction of the blood volume of at least 25 per cent.

It is interesting that Keith mentioned in the same report the fact that in some instances of failure following the use of gum acacia the gum solution itself had been faulty. It is believed that the condition of the patient at the time the wound is received has a great bearing on the manner in which the injury is tolerated. Cowell<sup>26</sup> stated: "In battle and at points of activity, the conditions of excitement, cold, thirst, fatigue, and possible loss of sleep become important pre-wound factors in initiation of shock." Wallace<sup>24</sup> called attention to the fact that "the soldier was, even in trench warfare, on a limited supply of water, and consequently there was no reservoir on which the circulation could draw in case of need. His condition in this respect much resembled that of a patient after the old fashioned preparation for operation." The effects of an inadequate supply were summarized by Robertson and Bock<sup>27</sup> as follows: "Blood volume tests made on a number of cases of hemorrhage have shown that in many instances dilution of the blood occurs very slowly. The principal reason for this lack of prompt dilution seems to be an initial marked diminution in the reserve fluid of the tissues and the lack of any subsequent attempt to make up the fluid deficiency." It is believed these observations indicate that the death of a person who is subjected to these unfavorable circumstances may occur when the amount of hemorrhage has been relatively small. No work which has been performed to date explains the death of soldiers in which there was no hemorrhage and no gross muscle injury. As has been stated previously, these instances are the exceptional ones. It should be remembered in considering the cases which were observed during the war that the studies which were made before and subsequent

25 Keith. Blood Volume in Shock. Report of Shock Committee, Medical Research Committee no. 26, pp. 31-44, March 1919.

26 Cowell. The Initiation of Wound Shock. Report of Shock Committee, Medical Research Committee no. 25, p. 168, December 1917.

27 Robertson and Bock. Memorandum on Fluid Volume after Hemorrhage. Report of Shock Committee, Medical Research Committee no. 25, p. 21, March 1918.

to the death of the patients were performed under abnormal conditions. Occasional deaths are unexplained in well regulated hospitals when more favorable circumstances for complete studies prevail. Undetected intracranial injuries or gas poisoning might have been the cause for some of the deaths in cases in which the etiology was not determined.

In civil practice, the conditions which attend the development of shock are usually less complicated than are those which were encountered during the war. Cold, fatigue, inadequate fluid and food supplies are usually absent. Many of the patients who are seen in a state of shock in civil practice have had an operation under an anesthetic. In some of these it is doubtful if there has been enough loss of fluid from the blood stream to account for the low blood pressure. Dale<sup>28</sup> showed in experiments on animals that less histamine is required to produce a low blood pressure if the animal is under an ether anesthetic or if hemorrhage has been produced. However, proof that the fall in blood pressure after injury to muscles is due to the formation of histamine is lacking. Previous studies by Blalock<sup>29</sup> and by Blalock and Bradburn<sup>30</sup> showed that the mechanism of the production of a low blood pressure is different after hemorrhage alone and after trauma to the central nervous system. It is believed from a consideration of these observations that all instances of a low blood pressure are not caused by the loss from the blood vessels of whole blood and plasma. The evidence presented in this paper indicates that the loss of fluid or of blood from the blood vessels or the accumulation of blood in dilated vessels occurs exclusively or almost exclusively in the area which has been traumatized. More concretely, the present experiments indicate that trauma to an extremity causes enough loss of blood volume locally to account for the reduction in the blood pressure and it is believed that the accumulation of blood and loss of fluid from the blood stream after intestinal trauma, for example, is limited almost entirely to the area which has been traumatized. The injection of histamine into the patent femoral artery of any extremity in which all of the venous return had been occluded, produced no greater alteration in the blood pressure than simple occlusion of the venous return. This indicates that the important factor in the production of hemorrhage when a tourniquet is placed on tightly enough to occlude the venous return, but not tightly enough to occlude the arterial inflow, is the head of arterial pressure and not the local formation of toxic products.

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28 Dale. Supplementary Note on Histamine Shock. Report of Shock Committee Medical Research Committee no 26, pp 15-18 March, 1919

29 Blalock. Mechanism and Treatment of Experimental Shock. I Shock Following Hemorrhage, Arch Surg 15 762 (Nov ) 1927

30 Blalock and Bradburn. Trauma to the Central Nervous System. Its Effects on Cardiac Output and Blood Pressure. An Experimental Study, Arch Surg 19 725 (Oct ) 1929

References have already been made in this discussion to the theories which maintain that nerve impulses or toxic products resulting from trauma initiate the decline in blood pressure. The theory of fat embolism was not supported either in these experiments or in those of Cannon.<sup>31</sup> Examination of the lungs in some of Cannon's experiments showed no accumulation of fat. The femur was not broken in most of the experiments reported here. This is not essential, however, as Lehman and Moore<sup>32</sup> showed that it is not necessary to fracture long bones or indeed to produce gross trauma of any kind in order to produce fat embolism. The fact that the local loss of blood volume accounted for the decline of pressure in the present experiments, shows that fat embolism if present was not the cause of the condition found.

The respirations were observed carefully in many of the experiments, and there was nothing to indicate that the shock was due to over-ventilation. The respirations were slow most of the time, and when they became slightly accelerated the amplitude decreased. The theory of acapnia found no support in the experiments of Cannon,<sup>31</sup> in which he found that shock could be produced by muscle injury even though the breathing was kept uniform by artificial means.

It has been shown<sup>33</sup> that shock is not produced by acidosis alone by the injection of acid into the blood stream until the alkali reserve was reduced to a low degree. The blood pressure did not fall to a shock level. Bayliss<sup>17</sup> found that the injection of lactic acid, after a low blood pressure had been produced by muscle injury, did not exaggerate the state and in some instances caused an elevation of the blood pressure. Conflicting results have been obtained by different observers<sup>34</sup> in studies of the epinephrine content of the blood when the blood pressure is at a low level. To produce a low blood pressure it is necessary to inject a much larger amount of epinephrine than is liberated by reflex stimulation.<sup>35</sup> The experiments of Mann<sup>36</sup> in which he found that the suprarenal glands can be removed without producing shock are evidence against the theory of suprarenal exhaustion. In regard to the part which infection may play in the development of shock Cannon<sup>37</sup> stated "Furthermore the state is commonly well established before infection, and therefore is not of bacterial origin." McNee, Shadden and McCart-

31 Cannon (footnote 3 p 147)

32 Lehman and Moore. Fat Embolism Including Experimental Production Without Trauma. Arch Surg **14** 620 1927

33 Acidosis and Shock. Report of Shock Committee. Medical Research Committee no 25 p 257, October 1918

34 Bedford and Jackson. Proc Soc Exper Biol & Med **13** 36 1916  
Stewart and Rogoff. Am J Physiol **48** 22 1919

35 Cannon (footnote 3 p 125)

36 Mann. Shock During Anesthesia. J A M A **69** 77 1917

37 Cannon (footnote 3 p 154)



ney<sup>23</sup> made studies on many wounds obtained during the war from the point of view of infection. They stated, "Bacterial infection, moreover, was shown to be unimportant in these wounds." No evidence to support any of these theories was found in the present experiments, since it was found that the local loss of blood volume was sufficient to account for the reduction in the blood pressure.

A great deal of work has been performed to determine the effects on the blood pressure of the injection of extracts of various tissues, of the products of autolysis of crushed muscle and of many other substances. Most of these substances caused a decline in the blood pressure. No evidence for the action of any of these products was found in the present experiments. Many of the substances which were studied are supposed to be fairly closely related to histamine. Goodpasture<sup>38</sup> found that a fresh extract of the pancreas produced changes in the gallbladder similar to those observed by Bradburn and Blalock<sup>14</sup> after the injection of histamine. Trauma to the extremities did not produce any alteration in the gallbladder.

It is believed that one should be guarded in drawing conclusions which apply to man from experimentation on animals, particularly if the latter have been anesthetized. Barbitol, the anesthetic which was used in these experiments, does not lessen greatly the amount of the loss of blood which is necessary for the production of a low blood pressure. Dale<sup>28</sup> found that a cat which had been anesthetized by ether for two hours would tolerate only one-fifth as much histamine without the production of death as would the same cat without an anesthetic. Concerning the effect of trauma to the anesthetized animal, he stated, "It seems in the highest degree probable that the sensitiveness of the animals to traumatic toxins has been thereby greatly enhanced." The effect of barbitol anesthesia on the tolerance to histamine has not been determined. Ether anesthesia causes little alteration in the amount of hemorrhage that is necessary for the production of a low blood pressure. If the results of these experiments had indicated that the decline in pressure following trauma to an extremity is due to a toxin, they would be received in a more skeptical light in view of Dale's work, which showed that anesthesia increases the susceptibility to histamine. Since the decline in pressure in the present experiments was due to the loss of a large part of the blood volume into the traumatized area, it is believed that similar results would be obtained on unanesthetized animals. Shock in the human being is usually associated with the loss of a great deal of fluid through sweating. This is not encountered in dogs because of the absence of sweat glands. It is fortunate in experiments of this type that such is the condition, because a more accurate idea can be gained as to the site of the loss of fluid from the blood stream.

# SUMMARY

All the experiments were performed on dogs, anesthetized by barbital. The blood pressure was determined frequently. The experiments were undertaken in order to test the various theories which have been advanced in an effort to explain the initiating agent in the development of a low blood pressure after gross trauma. In some experiments, the method of Cannon and Bixler, by which they produced a decline in blood pressure by traumatizing a posterior extremity, was employed. In other experiments their procedure was altered in various ways.

The following is a brief summary of the results:

1. The blood pressure could not be reduced to a shock level by trauma to one of the posterior extremities without causing the loss of a sufficient part of the blood volume into the traumatized area to account for the decline in the pressure. There was a greater proportionate loss of plasma than of red cells and this accounts for the concentration of the blood elsewhere.

2. The injection of histamine into the patent femoral artery of a thigh which was tightly constricted by a tourniquet, in some instances, caused a fall in blood pressure. After the uppermost part of the femur had been removed the injection of histamine into the artery did not cause a decline in pressure if the tourniquet was properly applied.

3. After the femoral artery had been freed in the groin and a tourniquet had been placed around the thigh constricting everything except the artery, no appreciable decline in pressure resulted whether the femur was or was not resected. The injection of histamine into the artery caused no greater alteration in the pressure than did the simple application of the tourniquet. The application of tourniquets to both thighs by the same method caused a marked fall in the blood pressure.

4. A fall in blood pressure to a low level was produced by trauma to an extremity, the thigh of which was constricted by a tourniquet, except for the femoral artery. A sufficient amount of hemorrhage occurred into the traumatized part to account for the decline in the blood pressure. This occurred whether the upper part of the femur had or had not been removed.

5. Removal of the tourniquet from a thigh, the structures of which had been constricted for a long time except for the femoral artery, caused a fall in the blood pressure. The same result was obtained whether there had or had not been trauma.

6. After the femoral artery and vein had been dissected free in the groin and a clip had been placed on the vein and a tourniquet which constricted all of the structures of the thigh except the artery and vein had been placed beneath the vessels, removal of the clip from the

vein usually did not cause a decline in the blood pressure. The same result was obtained whether there had or had not been trauma and whether the upper part of the femur had or had not been removed.

7 When the arterial inflow and the venous outflow to an extremity were entirely occluded, gross trauma to the extremity did not produce a decline in the blood pressure.

8 Massage of either the traumatized or the opposite nontraumatized extremity usually produced a temporary reduction in the blood pressure.

9 After the blood pressure had been lowered by trauma to an extremity, occlusion of the terminal aorta and vena cava was followed by a fall or a rise or no alteration in the blood pressure.

10 If the terminal abdominal aorta or vena cava of the dog had been occluded for an hour, release of the occlusion did not result in the production of a low blood pressure.

11 The transfusion of blood from one dog in which a low blood pressure has been produced by trauma to an extremity to another dog in which a low blood pressure had been produced by a loss of blood either outside the body or into the tissues of the body resulted in an elevation of the blood pressure in the recipient.

12 The intravenous injection of histamine caused definite alteration in the gallbladder. Trauma to any extremity did not produce these changes.

13 Trauma to an extremity did not cause a congestion of blood in the intestinal tract or the accumulation of free fluid in the peritoneal cavity.

The experiments which are presented in this paper offer no evidence that trauma to an extremity produces a toxin that causes a general dilatation of capillaries with an increase in capillary permeability and a general loss of fluid from the blood stream. Neither do they lend support to the other theories, such as fat embolism, acidosis, acapnia, suprarenal hyperactivity and hypoactivity and vasomotor exhaustion. There was a sufficient loss of blood volume into the traumatized area in all these experiments on dogs anesthetized by barbital to account for the reduction in the blood pressure. The time interval which elapsed between the initiation of the trauma and the reduction of the blood pressure to a shock level probably was not sufficiently great in these experiments to rule out the effects of decomposition products which are very slow in their actions. However, these experiments are comparable in the time required for the production of a low blood pressure with those of the other investigators whose theories have been discussed. It has been pointed out that definite conclusions cannot be drawn from these experiments as to the mechanism of the production of shock in man.

# BILIARY AND HEPATIC FACTORS IN PEPTIC ULCERS

AN EXPERIMENTAL STUDY \*

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Numerous investigators<sup>1</sup> observed the occurrence of peptic ulcers in animals following the diversion of duodenal secretions and attributed the development of these lesions to the loss of the neutralizing influence of the alkaline duodenal fluids on the acid gastric juice. Their conclusions were based on the work of Boldyreff - who promulgated the theory that gastric acidity was regulated by the regurgitation of the contents of the duodenum into the stomach. Boldyreff noted that the pancreatic juice was more alkaline than any of the other secretions that were present in the duodenum and he believed that it was the chief factor in the neutralization of the acid secreted by the stomach. The results of the investigations of MacLean and Griffiths,<sup>2</sup> McCann<sup>4</sup> and Yesko,<sup>5</sup> however, indicated that changes in gastric acidity did not depend on the regurgitation of alkaline duodenal juices. Recent determinations<sup>6</sup> of the gastric acidity in animals with pancreatic or bile fistulas showed that

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1 Hauser, G. Die peptischen schädigungen des Magens, des Duodenums und der Speiseröhre und das peptische postoperative Jejunalgeschwür in Henke and Lubarsch. Handbuch der speziellen pathologischen Anatomie und Histologie Berlin, Julius Springer 1926, vol 4. Bickel, A. Beobachtungen an Hunden mit exstirpierten Duodenum. Berl klin Wchnschr **46** 1201 (June 28) 1909. Esalto, J. Ulcus jejuni nach Gastroenterostomie, München med Wchnschr **58** 1144 (May 23) 1911. Mann, F. C. and Williamson, C. S. The Experimental Production of Peptic Ulcer, Ann Surg **77** 420 (April) 1923.

2 Boldyreff, W. Self Regulation of Acidity of Gastric Contents and Real Acidity of the Gastric Juice, Quart J Exper Physiol **8** 1 (April 14) 1914.

3 MacLean, H. and Griffiths, W. J. The Automatic Regulation of Gastric Acidity, J Physiol **66** 356 (Dec 20) 1928.

4 McCann, J. C. Studies on the Control of the Acidity of the Gastric Juice, Am J Physiol **89** 483 (Aug) 1929.

5 Yesko, S. A. The Effects of Ligation of Pancreatic Ducts on Gastric Digestion. Am J Physiol **86** 483 (Oct.) 1928.

6 Unpublished observations.

the acid values remained within the limits of normal variations for dogs, after biliary obstruction, the acidity was increased <sup>7</sup>

If Boldyreff's theory were correct, there would be a greater predisposition to the formation of peptic ulcers in animals which were deprived of their pancreatic juice than in those which were deprived of their bile. A survey of the literature revealed that ulcers were rarely reported after ligation of the pancreatic ducts or extirpation of the pancreas <sup>8</sup> but were observed frequently after biliary exclusion <sup>9</sup>. The following study deals with the experimental production of duodenal and gastric ulcers in dogs by interference with the flow of bile into the intestine and the possible significance of the results with respect to peptic ulcers in man.

#### METHODS

Under ether anesthesia and with aseptic precautions, biliary fistulas were established in a series of large dogs according to the method described by Rous and McMaster <sup>10</sup>. The common duct was ligated and divided near the intestine. A cannula attached to a rubber U-tube was inserted into the proximal end of the divided duct. The tube was brought out through the abdominal wall by means of a stab wound just below the costal margin. The free end of the drainage tube was then connected to a small glass T, to which a rubber collecting bag and a rubber outlet tube were attached. The whole apparatus was held in place by a protective dressing. This method permitted the collection of the total output of bile under sterile conditions and insured against the animals licking the fistulous openings. Accessory communications between the biliary tract and the intestine were ruled out at autopsy. The gallbladder was dealt with as follows. In some animals it was allowed to remain intact, in others the cystic duct was ligated and divided, in a number of dogs a cholecystectomy was performed, in one animal a cholecystostomy was done after ligation and division of the common duct.

7 Still, K. S., and Carlson, A. J. The Motor and Secretory Activity of the Stomach During Acute and Chronic Obstructive Jaundice in Dogs, *Am J Physiol* **89** 34 (June) 1929.

8 Minkowski, O. Untersuchungen über den Diabetes Mellitus nach Exstirpation des Pankreas, *Arch f exper Path u Pharmacol* **31** 85 (April 11) 1893.

9 Malkoff, G. M. The Pathology of Jaundice, St. Petersburg, Imperial Military Medical Academy, 1897. Simnitzky, quoted by Bogoras, N. Ueber Cholecystogastrostomie bei dem Magenulcus, *Arch f klin Chir* **134** 42 (Jan 26) 1925. Hosomi, K. Ueber das sogenannte peptische Geschwür des Magens und Duodenums beim Hunde, das gelegentlich der Choledochusplastik entsteht, *Virchows Arch f path Anat* **267** 726 (March 21) 1928. Kapsinow, R. Experimental Production of Duodenal Ulcer by Exclusion of Bile from the Intestine, *Ann Surg* **83** 614 (May) 1926. Bollman, J. L., and Mann, F. C. Chronic Duodenal Ulcers in Animals with Fck Fistulas on Certain Diets, *Arch Path* **4** 492 (Sept) 1927.

10 Rous, P., and McMaster, P. D. A Method for the Permanent Sterile Drainage of Intra-Abdominal Ducts as Applied to the Common Duct, *J Exper Med* **37** 11 (Jan) 1923.

Twenty-three dogs were studied and they were divided into three main groups. In group 1 the flow of bile from the fistula remained uninterrupted throughout the experiment. In group 2 at first the drainage of bile was free after the establishment of the fistula. Subsequently, however, obstruction developed and the flow of bile became intermittent or ceased. In group 3 the operation for fistula was unsuccessful from the beginning and complete biliary obstruction followed.

After prolonged drainage the bile usually became contaminated, but this did not seem to alter the secretion to any extent. All of the animals were kept on a diet low in fat. For control study, a series of fifty normal dogs was examined and no spontaneous ulcers of the duodenum or of the stomach were encountered. As another control study, nine dogs with pancreatic fistulas were observed over the following periods: seventeen, twenty, twenty-two, twenty-two, twenty-two, twenty-five, thirty, fifty-one and fifty-two days, respectively, and no lesions were found in the stomach or the duodenum.

#### EXPERIMENTAL OBSERVATIONS

**SERIES 1 Dog 509**—In a male mongrel, weighing 15 Kg, a bile fistula was produced, with cholecystectomy. Secretion continued throughout the experiment. The animal became extremely weak and emaciated and was found dead on the sixteenth day.

*Autopsy*—The dog weighed 12.1 Kg. A round, penetrating acute ulcer was found on the anterior surface of the duodenum opposite the ampulla of Vater.

**Dog 510**—In a dog, weighing 26 Kg, a bile fistula was produced, with cholecystectomy. The animal secreted large amounts of bile throughout the experiment. It began to vomit on the twelfth day, and was found dead on the fourteenth day.

*Autopsy*—The dog weighed 19.7 Kg. A few pockets of pus were found between the lobes of the liver, which was normal otherwise. On the anterior surface of the duodenum just below the pylorus, there was an acute, oval, penetrating ulcer measuring 2.5 by 1.5 cm, with irregular, undermined margins.

*Microscopic Examination*—Examination revealed an acute, penetrating ulcer, which involved all the layers of the duodenum down to the serosa. The margins were undermined. The surface of the ulcer was covered by an amorphous material. There was no cellular reaction.

The liver was normal, except for marked congestion of the capillaries in the central portions of the lobules. The pancreas and lungs also showed marked congestion of the blood vessels.

**Dog 511**—In a female mongrel, weighing 17.1 Kg, a bile fistula was produced, with cholecystectomy. Secretion continued throughout the experiment. The animal became progressively weaker and was found dead on the thirteenth day.

*Autopsy*—The dog weighed 13.2 Kg. Diffuse suppurative peritonitis was present. A punched out, perforated ulcer measuring 1.5 by 0.7 cm was found on the anterior surface of the duodenum 1.5 cm below the pylorus. The perforation was sealed over incompletely by omentum. The liver was normal except

for a fibrinopurulent exudate which covered the surface. The lungs showed consolidation of the right lower lobe. The spleen was small and contracted.

*Microscopic Examination*—There was an acute perforated ulcer extending through all the coats of the duodenum. The margins were sharply defined, and in the underlying tissues there was a moderate infiltration of polymorphonuclear leukocytes. Adjacent to the perforation, the base was formed by a thin layer of muscle and the fibrous wall of the biliary sinus tract. The surface of the ulcer was covered by cellular debris and polymorphonuclear leukocytes. The surface of the liver was covered by a fibrinopurulent exudate. The capillaries



Fig 1—Acute perforated duodenal ulcer in dog 511

in the central portions of the liver lobules were dilated, and the cords were compressed. The lungs showed lobar pneumonia.

*Dog 13-28*—In a male collie, weighing 188 Kg, a bile fistula was established, with the gallbladder intact. Secretion continued throughout the experiment. The animal became progressively weak and was killed on the twelfth day because of its poor condition.

*Autopsy*—The dog weighed 177 Kg. The wound was infected. In the duodenum there were two acute shallow ulcers, opposite one another. They were about 3 cm below the pylorus, the one on the anterior surface measuring 1.5 by 0.5 cm and the one on the posterior surface, 1 by 0.5 cm. The bases were

covered by a green slough. The mucosa of the duodenum was congested as far down as the main pancreatic orifice.

*Microscopic Examination*—Both ulcers were typical acute mucosal erosions of the duodenum extending down to the muscularis mucosae with polymorphonuclear and round cell infiltration of the underlying tissues.

Dog 21-28—In a female mongrel weighing 14.4 Kg. a bile fistula was produced with the gallbladder intact. The average daily output of bile was 78 cc. Secretion continued for fifty-three days then ceased. The animal was killed on the fifty-fifth day. No icterus was observed.

*Autopsy*—The dog weighed 10.4 Kg. No ulcers were found. The liver appeared normal. The gallbladder was of about normal size and was filled withropy golden yellow bile. The bile ducts were moderately dilated. The glass



Fig. 2 (dog 511)—Biliary fistula, thirteen days. Acute perforated duodenal ulcer. Reduced from  $\times 18$ .

U-tube was filled with thick, muddy, inspissated bile which probably interfered with the outflow of bile.

*Microscopic Examination*—The liver showed marked central fatty degeneration, pericholangitis and pericholangitic abscesses.

Dog 10-29—In a female airedale weighing 14.4 Kg. a biliary fistula was established, with cholecystectomy. The average daily output of bile was 64 cc. Bile was secreted during the entire period of experiment and the dog remained in excellent condition. It was killed on the fifty-second day.

*Autopsy*—The dog weighed 13.1 Kg. No gross abnormalities were observed. No ulcers were found. Microscopic examination was not made because of autolysis of the viscera.

Dog 22-29—In a male mongrel weighing 15.5 Kg. a biliary fistula was produced, with cholecystectomy. The average daily output of bile was 142.5 cc.



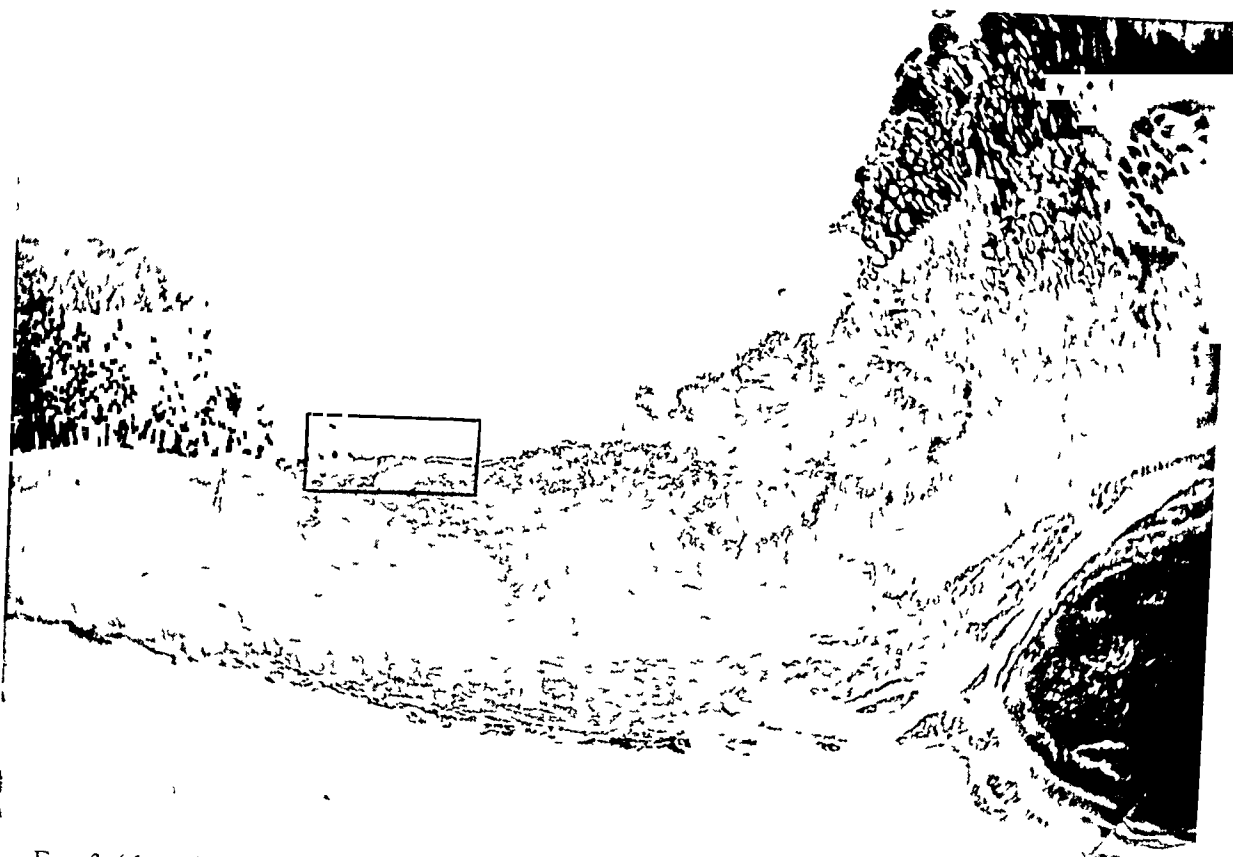


Fig 3 (dog 505) —Biliary fistula followed by biliary obstruction, twenty-nine days Chronic penetrating duodenal ulcer with evidence of healing Reduced from  $\times 21$  See figure 4



Fig 4 (dog 505) — Area included in square in figure 3 High power magnification shows the base of the ulcer filled in by newly formed connective tissue covered by regenerating epithelium Reduced from  $\times 180$

bile was secreted throughout the experiment, and the dog remained in excellent condition. It was killed on the one hundred and second day.

*Autopsy*.—The dog weighed 133 Kg. The liver appeared normal. There was no dilatation of the bile ducts, and the cannula was in situ. There were no ulcers of the stomach or duodenum. Numerous pinpoint cortical abscesses were found in the kidneys.

*Microscopic Examination*.—Microscopic examination revealed no abnormalities of the viscera except the kidneys which showed an occasional cortical abscess.

**SERIES 2 Dog 505**.—In a male collie weighing 182 Kg, a bile fistula was produced with ligation and division of the cystic duct. There was intermittent drainage. Bile was secreted for one week, the secretion then stopped for four days, started again for one week, stopped for one day and then continued until death which occurred suddenly on the twenty-ninth day.

*Autopsy*.—The dog weighed 137 Kg. Suppurative peritonitis was present. On the anterior surface of the duodenum just below the pylorus, there was an

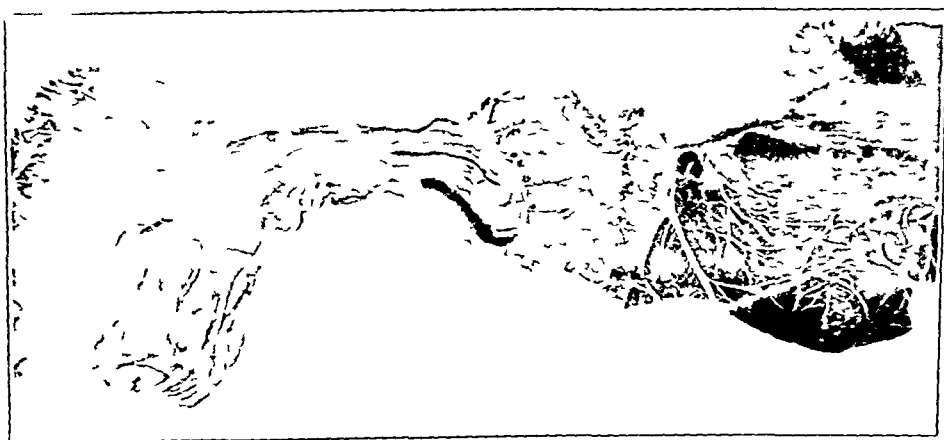


Fig. 5 (dog 506).—Cholecystostomy with intermittent drainage, fifty-six days. Large chronic perforated duodenal ulcer. Base formed by adherent omentum, pancreas and lymph node. Reduced from  $\times 6$ .

oval indurated penetrating ulcer measuring 1 by 0.5 cm. The liver was firm and icteric. The spleen was small and firm. The mesenteric lymph nodes were enlarged and soft. The pancreas was firm.

*Microscopic Examination*.—There was a chronic penetrating ulcer, with evidence of healing. The ulcer extended partly through the outer longitudinal muscular layer. The margins were sharply defined. The base showed a marked proliferation of connective tissue and infiltration with leukocytes. The surface of the ulcer was covered by regenerating epithelium. In the liver the bile canaliculi were dilated in the central portions of the lobules. Many of the Kupffer cells contained bile pigment. There were a few focal necroses and a moderate periportal infiltration with mononuclear leukocytes.

**Dog 506**.—In a male mongrel, cholecystostomy was performed, with ligation and division of the common duct. Drainage was intermittent due to contraction of the orifice of the fistula. During such periods 'white bile' was secreted. The animal became progressively weak and emaciated and died after fifty-six days.

*Autopsy*—The fistulous tract was patent. The mucosa of the gallbladder was normal. The common and hepatic ducts were dilated. The liver showed no gross changes. On the anterior surface of the duodenum, about 4 cm below the pylorus, there was an irregular indurated ulcer 2.3 cm in diameter, which had perforated, but the perforation was sealed over by adherent omentum and pancreas.

*Microscopic Examination*—A chronic ulcer was present, which involved all the layers of the duodenum. Beneath the abrupt margins, connective tissue proliferation and infiltration with polymorphonuclear leukocytes and round cells were found. The base of the ulcer was formed by adherent omentum,



Fig 6—Subacute duodenal and gastric ulcers in dog 507

pancreas and a lymph node, overlying these there was a layer of granulation tissue and leukocytes.

The liver showed dilated bile canaliculi and degeneration of the liver cells in the central areas of the lobules. The larger bile ducts were dilated.

*Dog 507*—In a male mongrel, weighing 20.8 Kg, a bile fistula was established, with ligation and division of the cystic duct. Secretion continued for twenty-six days, then diminished and finally ceased. The animal became progressively jaundiced and emaciated and was killed on the forty-sixth day.

*Autopsy*—The dog weighed 12 Kg. Three ulcers were found, two gastric and one duodenal. The duodenal ulcer was punched out and measured 0.5 by 0.3 cm. It was on the anterior surface just below the pylorus. The gastric ulcers occurred

on the lesser curvature 4.5 and 5.5 cm. respectively above the pylorus. Both were penetrating ulcers with undermined margins and one of them had perforated the perforation being sealed over by omentum. They measured 1.7 by 1 cm. and 1.7 by 0.5 cm. respectively. The liver was firm and icteric. The larger

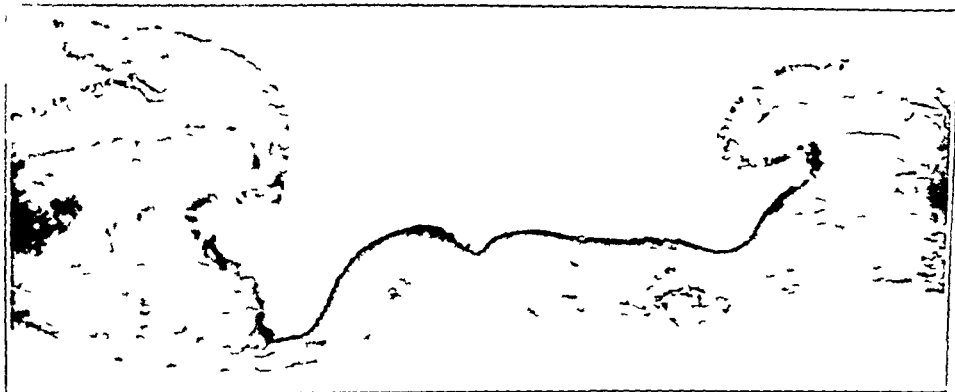


Fig 7 (dog 507) —Biliary fistula followed by biliary obstruction forty-six days. Subacute gastric ulcer with overhanging edges. Reduced from  $\times 13\frac{1}{2}$

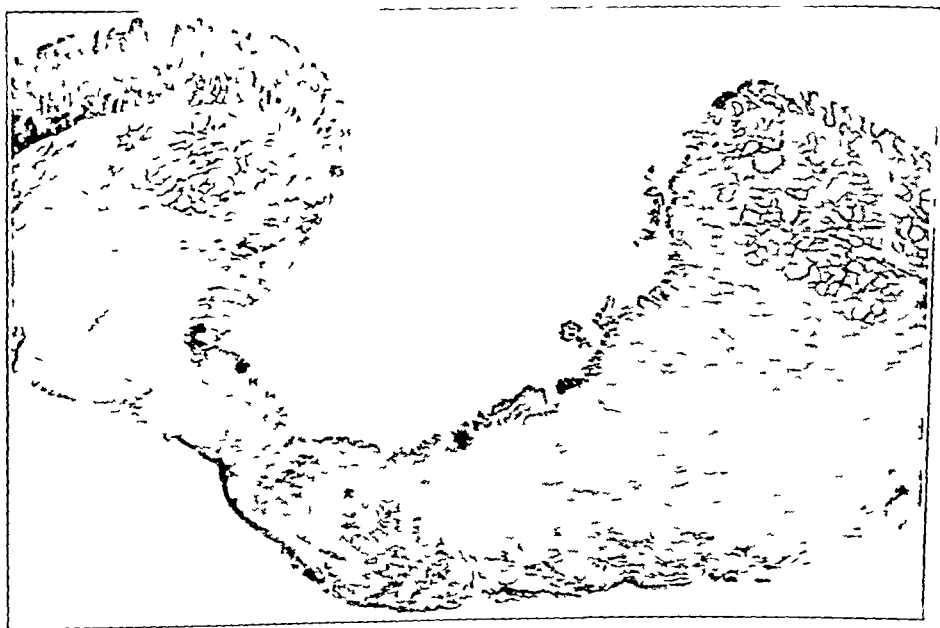


Fig 8 (dog 507) —Biliary fistula followed by biliary obstruction forty-six days. Subacute duodenal ulcer. Reduced from  $\times 25$

bile ducts were dilated, and a stricture was found in the common duct just above the cannula. The regional lymph nodes were enlarged and icteric. The right lung was completely consolidated; the left showed patchy consolidation.

*Microscopic Examination*—The duodenal ulcer was of the subacute penetrating type with abrupt margins. It extended through all the layers of the

intestine down to the serosa. The surface of the ulcer was covered by a purulent exudate of polymorphonuclear leukocytes and round cells which infiltrated the underlying structures. The base was formed by newly formed connective tissue. The serosa opposite the ulcer was thickened and contained proliferating fibroblasts, capillaries and numerous polymorphonuclear leukocytes. The gastric ulcers had similar histologic characteristics, one had perforated. The margins were undermined, and the base was formed by newly formed connective tissue covered by a cellular exudate. The serosa showed the same reaction as in the duodenal ulcer. In the liver, the larger bile ducts were dilated and the small bile canaliculi were distended near the centers of the lobules. The Kupffer cells in this region contained bile pigment. Pericholangitis, pericholangitic abscesses and focal necroses were present. There was also some periportal fibrosis. The lungs were the seat of a hemorrhagic pneumonia. In the kidneys, there was a hemorrhagic exudate in the glomeruli with numerous thrombi in the capillaries.

Dog 508—In a male terrier, weighing 19.5 Kg, a bile fistula was established, with ligation and division of the cystic duct. Secretion continued for sixteen days, then ceased. The animal was found dead on the twenty-sixth day.

*Autopsy*—The dog weighed 14.1 Kg. Suppurative peritonitis due to a perforated duodenal ulcer was found. A punched out, indurated ulcer, measuring 2 by 1.2 cm, was found on the anterior surface of the duodenum, 1.5 cm below the pylorus. In the base there was a small perforation. There was autolysis of the other organs.

*Microscopic Examination*—The ulcer that had perforated was of the chronic type. Its margins were abrupt, and the base was formed by connective tissue. The underlying tissues were infiltrated by polymorphonuclear leukocytes and round cells. The surface was covered by amorphous material and cellular debris.

Dog 512—In a male mongrel, weighing 13 Kg, a bile fistula was produced, with cholecystectomy. Secretion continued for nine days, then became intermittent and finally ceased on the twenty-seventh day. The animal was icteric and in good condition when it was killed on the forty-first day.

*Autopsy*—The dog weighed 10.3 Kg. The liver was firm and icteric. The bile ducts were dilated. No ulcers were found. Microscopic examination was not made.

Dog 17-28—In a male airdale, weighing 17.8 Kg, a bile fistula was established, with the gallbladder intact. The average daily secretion of bile was 94 cc. Secretion continued for thirty days, then ceased. The animal became jaundiced and was found dead on the thirty-sixth day, following an exploratory laparotomy.

*Autopsy*—The dog weighed 17.2 Kg. There were diffuse suppurative peritonitis and marked autolysis of all the organs. A stricture of the common duct was found just above the cannula. No ulcers were found. No microscopic examination was made because of autolysis of the organs.

Dog 18-28—In a male collie, weighing 12.5 Kg, a biliary fistula was established, with the gallbladder intact. The average daily output of bile was 62.5 cc. Secretion continued for sixty-five days, then icterus was noted, and the animal was killed on the sixty-seventh day.

*Autopsy*—The weight was 9.6 Kg. There was a small, oval erosion of the mucosa of the duodenum 2 cm below the pylorus. The liver was icteric, and contained numerous small abscesses. The bile ducts and gallbladder were distended withropy, turbid, dark green bile. The glass cannulas were filled with inspissated dark brown bile which probably interfered with the free outflow of bile and caused a partial obstruction.

*Microscopic Examination*—The lesion in the duodenum was a shallow small mucosal erosion. The changes were not sufficiently marked to be considered a true ulcer and the lesion was not included in the results. Dilated bile canaliculi, proliferation of the smaller bile ducts, pericholangitis and pericholangitic abscesses were found in the liver. Numerous focal necroses and a few infarcts were also present. The gallbladder showed no changes.

*Dog 2-29*—In a male mongrel, weighing 17 Kg, a bile fistula was established with the gallbladder intact. The average daily output was 119 cc. After seven-and-a-half days of continuous secretion, an exploratory operation was performed. No ulcer was palpable in the stomach or duodenum. The liver and biliary tract appeared normal. The gallbladder contained a small amount of thick, dark, viscid brown bile. A cholecystectomy was performed at this time. Following the operation, jaundice developed and the secretion of bile stopped. The animal was killed seven days afterward.

*Autopsy*—The dog weighed 15.3 Kg. Diffuse suppurative peritonitis was present. On the anterior surface of the duodenum, 1.5 cm below the pylorus there was a round, punched out ulcer measuring 1 cm in diameter. The base was covered with slough. The liver was jaundiced, the bile ducts were dilated and inspissated bile filled the lumen of the U-tube, which probably accounted for the development of the obstruction. There was no stricture of the common duct.

*Microscopic Examination*—There was a duodenal ulcer of the subacute penetrating type, with abrupt margins, involving the inner circular and part of the outer longitudinal coats. The surface was covered by a purulent exudate. In the base there was newly formed connective tissue. The underlying tissues were infiltrated by polymorphonuclear leukocytes. Overlying the ulcer, the serosa was thickened and contained proliferating capillaries and young fibroblasts. The bile canaliculi of the liver were distended especially in the central portions of the liver lobules. The Kupffer cells contained bile pigment. No other changes were observed.

*Dog 3-29*—In a male collie weighing 16.9 Kg, a bile fistula was produced, with the gallbladder intact. The average daily secretion of bile was 114.5 cc. Secretion continued for thirty-six days, then ceased. The animal became jaundiced and was killed on the forty-first day.

*Autopsy*—The dog weighed 13.4 Kg. The liver was firm. The gallbladder and bile ducts were dilated, and a stricture of the common duct was found just above the cannula. No ulcers were found.

*Microscopic Examination*—The liver showed dilated bile canaliculi in the central portions of the lobules, pericholangitis and multiple abscesses.

*Dog 15-29*—In a male terrier, weighing 14.6 Kg, a bile fistula was established with cholecystectomy. The average daily secretion of the bile was 123 cc. Secretion continued uninterrupted throughout the experiment until the last few days when a slight icterus of the conjunctivae was noted. The animal was killed on the sixty-ninth day. The general condition was excellent throughout the experiment.

*Autopsy*—The dog weighed 16 Kg. The liver was firm and icteric. The bile ducts were not dilated, the cannula was in place and there was no stricture. The cause for the icterus was not determined, possibly there was a partial obstruction due to inspissation of bile in the lumen of the U-tube. No ulcers were found.

*Microscopic Examination*—The liver showed dilatation of the bile canaliculi in the central portions of the lobules, proliferation of the smaller bile ducts and pericholangitis.

Dog 34-29—In a female mongrel, weighing 17.1 Kg, a bile fistula was produced, with cholecystectomy. The average daily output of bile was 126 cc. Bile was secreted throughout the experiment, with some diminution toward the end. The conjunctivae showed some jaundice at this time. The general condition remained excellent. The animal was killed with ether on the ninety-ninth day.

*Autopsy*—The tissues were icteric. The liver was small, firm and jaundiced. The common and hepatic ducts were dilated. Thick turbid bile was found in the ducts. One of the hepatic ducts was completely obstructed by the tube and cannula. In the stomach, on the lesser curvature 4 cm. below the cardia, there was a shallow irregular ulcer with overhanging edges measuring 2 by 0.5 cm. In addition, there were numerous smaller erosions in the fundus and one just above the pylorus. In the duodenum, just below the pylorus on the anterior surface, there was an irregular stellate shallow ulcer 1 by 0.5 cm. On the posterior surface of the duodenum, there was a small erosion about 0.3 cm. in diameter. The lymph nodes at the hilus of the liver were enlarged and icteric.

*Microscopic Examination*—The gastric and duodenal lesions were typical mucosal erosions without any cellular reaction. The liver showed distended bile canaliculi in the central portions of the lobules, pericholangitis, periportal fibrosis, proliferation of the smaller bile ducts and focal necroses. The Kupffer cells contained bile pigment. The larger bile ducts were dilated.

Serif 3, Dog 7-28—In a female collie, weighing 13 Kg, a bile fistula was established, with the gallbladder intact. The fistula did not function. The animal became progressively weak and jaundiced and was killed on the thirty-third day because of its poor condition.

*Autopsy*—There was marked jaundice. The liver was shrunken, soft and deeply icteric, with numerous small abscesses. The spleen was small and of rubbery consistency. There was old blood in the stomach, but no ulcers were found. The gallbladder and ducts were markedly distended with thick, viscid bile. There was a stricture of the common duct above the cannula.

*Microscopic Examination*—The liver showed distended bile canaliculi, proliferation of the smaller bile ducts, pericholangitis and pericholangitic abscesses. The Kupffer cells contained bile pigment.

Dog 12-28—In a male airedale, weighing 19 Kg, a biliary fistula was produced with the gallbladder intact. There was a small irregular secretion which ceased completely on the fourteenth day. The animal became progressively jaundiced and was found dead on the fifty-seventh day.

*Autopsy*—The animal was thin and jaundiced. The bile ducts and gallbladder were dilated because of a stricture of the common duct above the cannula. The liver was firm and icteric. The heart muscle was flabby. No ulcers were found.

*Microscopic Examination*—The liver showed distended bile canaliculi, proliferation of the smaller bile ducts and periportal fibrosis. The capillaries in the central portions of the lobules were dilated, and the liver cords were compressed.

Dog 5-29—In a female collie, weighing 15.7 Kg, a biliary fistula was established, with cholecystectomy. The fistula did not function. The dog remained in excellent condition throughout the experiment, although jaundice was marked. The animal was killed with ether on the one hundred and eighty-ninth day.

*Autopsy*—The dog weighed 14.4 Kg. On the anterior surface of the duodenum 1 cm. below the pylorus there was a penetrating, indurated ulcer measuring 1.5 cm. in diameter. The liver was small, firm and icteric. The larger bile ducts were dilated and contained pus. There was a stricture of the common duct just above the cannula. The mesenteric lymph nodes were enlarged.

*Microscopic Examination*—There was a chronic duodenal ulcer, with evidence of healing. The ulcer extended through Brunner's glands and the inner circular layer down to the outer longitudinal muscular coat. The surface was covered by a layer of polymorphonuclear leukocytes which infiltrated the underlying tissues. The crater was filled in by connective tissue. Along the edges of the ulcer there was an outgrowth of new epithelium. The liver showed distended bile canaliculi in the central portions of the lobules, proliferation of the smaller bile ducts and an increase of the periportal connective tissue. The Kupffer cells contained bile pigment. Occasional large abscesses containing numerous pigment-laden phagocytes were also found in the liver.

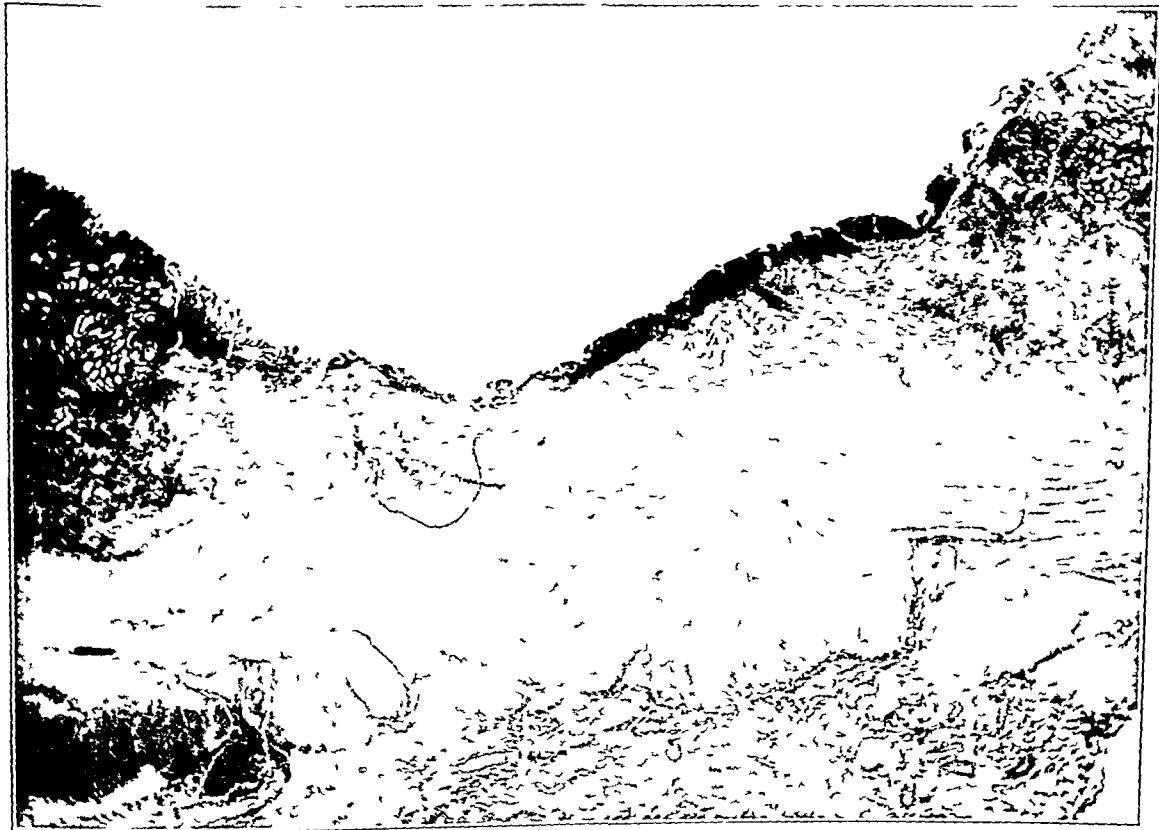


Fig 9 (dog 5-29)—Biliary obstruction, 189 days. Chronic duodenal ulcer with evidence of healing. The base is filled in by connective tissue. Reduced from  $\times 24$ .

**DOG 11-29**—In a female collie weighing 16.4 Kg a biliary fistula was established with cholecystectomy. The fistula did not function. The dog became progressively emaciated and jaundiced and was found dead on the forty-seventh day.

*Autopsy*—Intense jaundice and marked ascites were present. The peritoneal fluid was a turbid yellow. A chronic perforated ulcer with indurated overhanging edges, measuring 2 by 0.5 cm, was found on the anterior surface of the duodenum 2 cm below the pylorus. Another similar ulcer measuring 2 by 2.5 cm was





Fig 10 (dog 11-29) —Biliary obstruction, forty-seven days. Two chronic perforated duodenal ulcers, with evidence of attempted healing in one of them. Reduced from  $\times 12$ . See figure 11.

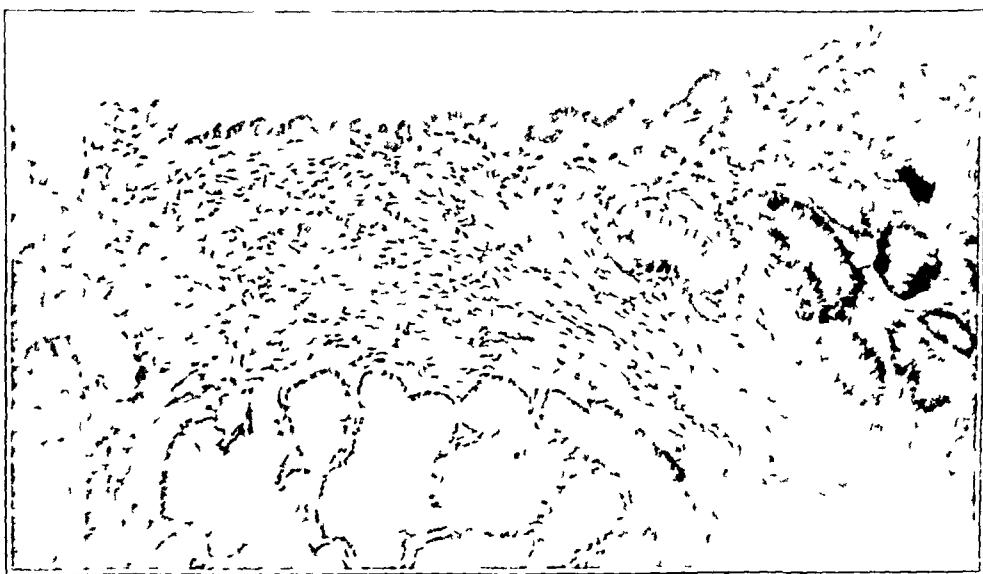


Fig 11 (dog 11-29) —Area included in square in figure 10. High power magnification shows proliferating fibroblasts covered by regenerating epithelium. Reduced from  $\times 180$ .

round on the posterior wall of the duodenum in the region of the ampulla of Vater and adherent to the pancreas. In the antrum of the stomach there were multiple mucosal erosions. The liver was small, firm and jaundiced. The larger bile ducts were greatly dilated and there was a stricture of the common duct above the ampulla. (When the ulcer was cut through in the region of the ampulla, a ligature was encountered at the site of the intramural portion of the common duct.)

*Microscopic Examination*—The histologic characteristics of both ulcers were similar. They were chronic perforated lesions with evidence of attempted healing.



Fig. 12 (dog 23-29)—Biliary obstruction 108 days. Gastric erosion with hemorrhage, inflammatory reaction in submucosa. Reduced from  $\times 30$ .

in one of them. The edges of the ulcers were overhanging and the surface was covered by amorphous cellular debris and polymorphonuclear leukocytes. Along one edge of the anterior ulcer there was a row of new proliferating epithelial cells. The base of this ulcer was formed by connective tissue. The base of the posterior ulcer was formed by connective tissue, pancreas, a lymph node and the wall of the sinus tract. In the antrum there were numerous areas in which the surface epithelium of the villi was destroyed. The villi were small and coalesced and stained homogeneously. There was no cellular reaction. The

liver showed dilatation of the bile canaliculi in the central portions of the lobules and central fatty degeneration of the liver cells. The Kupffer cells contained bile pigment.

Dog 23-29 —In a male airedale, weighing 15 Kg, a biliary fistula was produced with cholecystectomy. Secretion continued for ten days, then stopped, and icterus appeared. Toward the end of the experiment, marked ascites, edema of the legs and hematemesis developed. The animal was killed on the one hundred and eighth day because of its poor condition.

*Autopsy*—The tissues showed marked icterus. A large amount of clear, straw-colored fluid was present in the abdominal cavity. In the stomach, there were multiple acute ulcers in the antrum and on both sides of the magenstrasse. They varied in size from a few millimeters to 1.5 cm and were found in the crypts between the folds of mucous membrane. They were covered with fresh blood clots. There were no lesions in the duodenum. The heart muscle was flabby. The mesenteric lymph nodes were hemorrhagic and enlarged. The kidneys were pale and contained cortical infarcts. The liver was greatly diminished in size, firm and icteric. The larger bile ducts were dilated, and there was a complete stricture of the common duct above the cannula.

*Microscopic Examination*—The gastric lesions were erosions that extended through the mucosa and muscularis mucosae down to the inner circular layer. They occurred in the crypts between adjoining rugae. Sometimes the mucosa of the tops of the rugae remained intact, whereas in the depths there was extensive destruction of the epithelium. There was considerable undermining of the margins. The surface of the erosions was covered by blood clot, beneath which there was a layer of necrotic epithelium and leukocytes. In the underlying tissues, there was evidence of an intense inflammatory reaction with marked edema and fibrin deposit, infiltration with polymorphonuclear leukocytes and dilated capillaries and lymphatics. In the liver, the bile canaliculi were distended in the central portions of the lobules. There was proliferation of the smaller bile ducts and a marked increase of connective tissue causing extensive scarring and distortion of the liver lobules. There were numerous focal necroses and large cholangitic abscesses as well as pericholangitis and cholangitis of the larger bile ducts. The smaller ducts were not involved in the inflammatory process. The kidneys showed an occasional cellular cortical scar.

#### SUMMARY OF EXPERIMENTAL RESULTS

GROUP 1—*Uncomplicated Biliary Fistulas*—Seven animals were included in this series and were observed for periods extending from twelve to 102 days. Acute duodenal lesions were found in four dogs that died from twelve to sixteen days after the establishment of the fistulas. (One dog, 13-28, was killed on the twelfth day because of its poor condition.) In three animals, 509, 510 and 511, the lesions were single acute ulcers on the anterior wall of the duodenum. In one dog, 13-28, two erosions were found, one on the anterior and the other on the posterior surface. Perforation of the ulcer in dog 511 caused peritonitis and death. The three animals in which no lesions were found remained in good condition and were killed after fifty-two, fifty-three and 102 days respectively.

The histologic examination of the livers of the animals in this group revealed few changes. In one dog 21-28 the liver showed central fatty degeneration, pericholangitis and multiple abscesses.

GROUP 2—*Biliary Fistulas Followed by Biliary Obstruction*—Eleven animals were included in this series and were observed for periods extending from twenty-six to ninety-nine days. In six lesions were found after twenty-six, twenty-nine, forty-six, fifty-six, eighty and ninety-nine days respectively. In three dogs 505, 506 and 508, single chronic ulcers were found on the anterior surface of the duodenum. In one dog 2-29 a single subacute perforated duodenal ulcer was found on the anterior wall. In another dog 34-29 there were multiple erosions of the stomach and duodenum. In dog 507 there were multiple subacute ulcers, one in the duodenum and two in the stomach, one of the latter had perforated. The ulcer in dog 505 showed evidences of healing.

The histologic examination of the livers of the animals in this group revealed changes that were associated with moderate biliary obstruction. Abscesses of the liver were found in three dogs 507, 18-28 and 3-29, pericholangitis was found in one dog, 15-29.

GROUP 3—*Biliary Obstruction*—Five animals were included in this series and were observed for periods extending from thirty-three to 189 days. In three lesions were found after forty-seven, 108 and 189 days respectively. In one dog 23-29, multiple gastric erosions were encountered. In another dog 11-29, there were two perforated chronic duodenal ulcers. In the third animal 5-29 there was a single chronic ulcer on the anterior surface of the duodenum. The ulcers in dogs 11-29 and 5-29 showed evidences of healing.

The histologic examination of the livers of all of the animals in this group showed changes caused by prolonged obstruction of the larger bile ducts. Abscesses of the liver were found in three dogs 7-28, 5-29 and 23-29.

#### COMMENT

In a series of twenty-three dogs with various types of biliary exclusion, thirteen developed duodenal or gastric lesions. In ten animals ulcers were found in the duodenum, in two multiple gastric erosions occurred and in one dog, both gastric and duodenal ulcers were observed.

It is interesting to note that a chronic duodenal ulcer was observed in dog 508 after an interval of twenty-six days. A similar observation was made by Mann and Williamson<sup>11</sup>. This suggests the possibility that in man gastric and duodenal ulcers that have the histologic characteristics of chronic lesions may develop within a short period of time.

The condition of the gallbladder had no constant relationship to the incidence of ulcers. In groups 1 and 2 lesions occurred in animals with

<sup>11</sup> Mann and Williamson (footnote 1, fourth reference).

intact gallbladders, with ligation of the cystic duct and with cholecystectomy In group 3, ulcers were found only in the dogs whose gallbladders had been removed

Abscesses of the liver and pericholangitis occurred in some of the animals, but these lesions did not seem to have any influence on the development of ulcers

#### INCIDENCE OF ULCERS AND ENVIRONMENT

The animals in groups 1 and 2 were studied under different environmental conditions During the early part of the investigation, dogs 509, 510 and 511 of group 1, and 505, 506, 507 and 508 of group 2 were kept in old laboratory quarters It was difficult to maintain cleanliness, and the floors were damp because of inadequate drainage Although the constituents of the food were mixed and the quantity was plentiful, the preparation was poor and the utensils were insanitary The ingredients of the food had to be changed frequently because the animals refused to eat They lost weight rapidly and died early Under these conditions, the incidence of ulcers was nearly 100 per cent On the other hand, during a later period of the investigation, dogs 13-28, 31-28, 10-29 and 22-29 of group 1, and dogs 17-28, 18-28, 2-29, 3-29, 15-29 and 34-29 of group 2 were housed in new quarters The cages were kept dry and clean The diet was prepared carefully in clean utensils The dogs remained in good condition and lived for relatively long periods Under these improved conditions the incidence of ulcers dropped to 30 per cent

Although this was a small series of animals, it was noteworthy that in an unfavorable environment the incidence of ulcers was much higher than that under more favorable conditions It was not possible to make a similar comparative study of the animals of group 3 because most of them were studied only in favorable surroundings Nevertheless, ulcers developed in 60 per cent of the animals in this group

#### RÔLE OF MUCUS

The mechanism by which the exclusion of bile predisposes the mucosa to ulceration depends probably on the loss of some constituent in the bile which is essential for the maintenance of an intact surface epithelium The component of the bile that can serve this purpose most readily is the mucus because of its physicochemical properties Beaumont,<sup>12</sup> Claude Bernard<sup>13</sup> and Pavlov<sup>14</sup> observed that the healthy

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<sup>12</sup> Beaumont, W Experiments and Observations on the Gastric Juice and the Physiology of Digestion, Plattsburgh, F P Allen, 1833, p 103

<sup>13</sup> Bernard Claude Physiologie experimentale, Paris, J B Bailliere et fils, 1856, vol 2, p 408

<sup>14</sup> Pavlov, I The Work of the Digestive Glands London Griffin & Company, 1910 p 238

mucosa was always covered by a layer of mucus and suggested the protective function of this secretion. It is noteworthy that the duodenum which receives the acid gastric fluids and requires more protection for its surface epithelium than any other segment of the gastro-intestinal tract is supplied with mucus derived from four sources: the bile, the pancreatic juice, the intestinal mucous glands and Brunner's glands.<sup>14</sup> The pyloric region is composed entirely of mucous glands.<sup>14</sup> The relative importance of the mucus contained in the bile compared to the mucus in the other duodenal fluids is unknown but there is probably a close interrelationship between them. One of the effects of biliary exclusion may be the disturbance of the regulatory mechanism of mucous secretion which exposes the surface epithelium to the action of the gastric juice.<sup>17</sup>

#### CONCLUSIONS

The results of this investigation suggest the possibility that alterations in the function of the liver and in the secretion of bile may be important factors in the etiology of peptic ulcers. Although gross or microscopic changes in the biliary tract are found in only a small percentage of cases of ulcer in man,<sup>15</sup> nevertheless functional disturbances that are not recognized by present inadequate methods may exist. The periods of remission and exacerbation that characterize so-called chronic ulcers may coincide with intermittent functional alterations in the stomach and duodenum in response to changes in the liver and biliary system. If peptic ulcers are associated with deficiency of the liver in man, the administration of liver may be of therapeutic value. A clinical study is in progress to determine the efficacy of this form of treatment. The results obtained from these preliminary studies suggest that treatment with liver does have a beneficial effect, but the studies have not been carried on for a sufficient length of time to enable us to form definite conclusions.

15 Bensley, R. R. *The Structure of the Glands of Brunner*. Decennial Publications, University of Chicago, 1903, vol. 10, p. 279.

16 Bensley, R. R. *The Structure of the Mammalian Gastric Glands*, *Quart. J. Micr. Sc.* **41** 361 (Nov.) 1898. Lim, R. K. S. *The Gastric Mucosa*, *Quart. J. Micr. Sc.* **66** 187 (June) 1922.

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## DIAPHRAGMATIC ADHESIONS \*

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In this paper I shall point out in what manner adhesions between the diaphragm and the wall of the chest can act to further the healing of pulmonary tuberculosis and how, in their presence, the production of diaphragmatic paralysis may be harmful rather than beneficial

As a basis for this consideration, one must accept the fundamental proposition that movement of a tuberculous lung discourages healing while rest favors it

Since the time of Galen there has been active discussion concerning the effect of contraction of the diaphragm on the ribs to which it is attached Galen<sup>1</sup> believed that it raised them slightly Borelli<sup>1</sup> and later von Haller<sup>1</sup> were of the opinion that it tended to draw them downward In 1853, Duchenne,<sup>2</sup> of Boulogne, presented the results of experiments on dogs, horses and human beings, which seemed convincing substantiation of the earlier conception of Galen In 1896, Gerhardt,<sup>3</sup> while admitting the probable correctness of Duchenne's views, called attention to the fact that anything tending to lower the dome of the diaphragm or to raise its attachment to the wall of the chest might so change the direction of its pull on the ribs as to draw them downward on inspiration Between 1918 and 1924, Hoover,<sup>4</sup> reported the results of numerous clinical observations and experiments on dogs which directly controverted those of Duchenne and substantiated the observations of Borelli, von Haller and Gerhardt

The essence of Hoover's conclusions is that the contracting diaphragm exerts a medianward rather than an upward pull on the lower ribs, and consequently acts as an antagonist of the muscles tending to elevate and spread them He observed repeatedly in human beings and dogs that paralysis of the hemidiaphragm was followed by an increased upward movement of the lower ribs on the affected side and a widening of the subcostal angle Stimulation of the nerve caused a narrowing

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\* Submitted for publication, Oct 20, 1929

1 Galen, Borelli, and von Haller, cited by Duchenne Union Med **7** 105, 1853

2 Duchenne Union Med **7** 105, 1853

3 Gerhardt Ztschr f klin Med **30** 37, 1896

4 Hoover, C F The Functions of the Diaphragm and Their Diagnostic Significance, Arch Int Med **12** 214 (Aug) 1913

of the lower part of the thorax except in the exception which the dog had a very small subcostal angle and a high diaphragm.

He maintained that under normal conditions the muscles tending to elevate the ribs were able to overcome the antagonism of the diaphragm but in his clinical observations he found in accord with Gerhardt that pathologic factors tending to lower the dome of the diaphragm or raise its attachment to the ribs so increased its medianward pull that the lower ribs were drawn medianward on inspiration. He noted especially that high adhesions between the diaphragm and the wall of the chest could bring about this paradox.

Experimental and clinical observations of my own (to be published soon) have in the main substantiated the work of Hoover.

The diaphragm arising from the six lower ribs, the lumbar vertebrae and the ensiform cartilage, arches upward and medianward to its insertion in the central tendon. It is maintained in its domelike shape by the negative intrapleural pressure, the pericardial ligaments, the positive intra-abdominal pressure and the support of the abdominal viscera. For a considerable distance above its origin its upper surface coheres to the thoracic wall. Neither its origin nor its insertion are fixed points. Contracting thus around an arc, in what direction it exerts its force on the ribs to which it is attached must depend on the ratio between the height and the breadth of the arch. The higher the dome, the more the pull will be upward, the lower the dome, the more medianward. At the beginning of inspiration the upward factor must be at its maximum. As inspiration proceeds and the dome descends and the ribs rise, the median pull must increase proportionately.

From this it is obvious that adhesions between the diaphragm and the wall of the chest make more direct the medianward pull by raising the origin of the muscle, and so decreasing the height of the arch. Not only do they bring the diaphragm into more direct antagonism to the muscles tending to elevate the ribs, but they limit the descent of the diaphragm itself. They act thus to decrease both costal and diaphragmatic breathing. If, as not infrequently happens, the adhesions are on a level with the dome, or even higher, the diaphragm is wholly prevented from descending, and the entire force of its contraction is exerted in drawing the ribs downward and medianward with the result that on inspiration they are moved paradoxically in this direction. The adhesions prevent descent of the diaphragm and the diaphragm prevents expansion of the bony thorax. The resulting immobility must be assumed as being favorable to the healing of tuberculous lesions.

If, under these conditions, the diaphragm is paralyzed by extraction of the phrenic nerve respiration in the lung must be increased. The



diaphragm, fixed already in an expiratory position and contributing little to respiration, has been functioning chiefly in restricting the movement of the ribs. Its paralysis serves only to mobilize the ribs and allow them to function normally. It does not throw the dome into a higher position or alter appreciably its excursion.

#### REPORT OF CASES

CASE 1—Mr J. L., single, an American laborer, aged 40, came to the dispensary of the Research and Educational Hospital complaining of the usual symptoms of pulmonary tuberculosis of two years' duration. A year before, he had developed pleurisy with effusion of the left lung and had been treated by repeated aspirations. Physical, roentgen and sputum examinations confirmed the diagnosis of bilateral pulmonary tuberculosis. The roentgenogram showed high adhesions between the left side of the diaphragm and the thoracic wall. Examination with the fluoroscope showed no descent of the left diaphragm. On physical examination, it was found that movement of the ribs throughout the left thorax was markedly restricted, and that on inspiration the lower ribs moved downward and inward, paradoxically. The patient complained of inspiratory pain in this region.

On March 2, 1929, the left phrenic nerve was extracted. Observation of the respiratory movements after the operation revealed a marked increase in the movement throughout the affected side. The lower ribs now moved in the normal direction on inspiration, and the pain which had been present previous to the operation had disappeared. There was little, if any, further elevation of the diaphragm.

CASE 2—Mr J. C., single, American, an office worker, aged 30, entered the Research and Educational Hospital of the University of Illinois, complaining of a draining sinus of the left axillary region. On the basis of clinical and roentgenologic examinations, a diagnosis of chronic empyema was made. Following a course of irrigations, he was operated on, and a cavity was found which was bounded below by the diaphragm and extended upward and posteriorly under the scapula. The ribs and the intercostal tissues overlying it were resected, and the wound was packed. Healing progressed satisfactorily, except that a small sinus persisted.

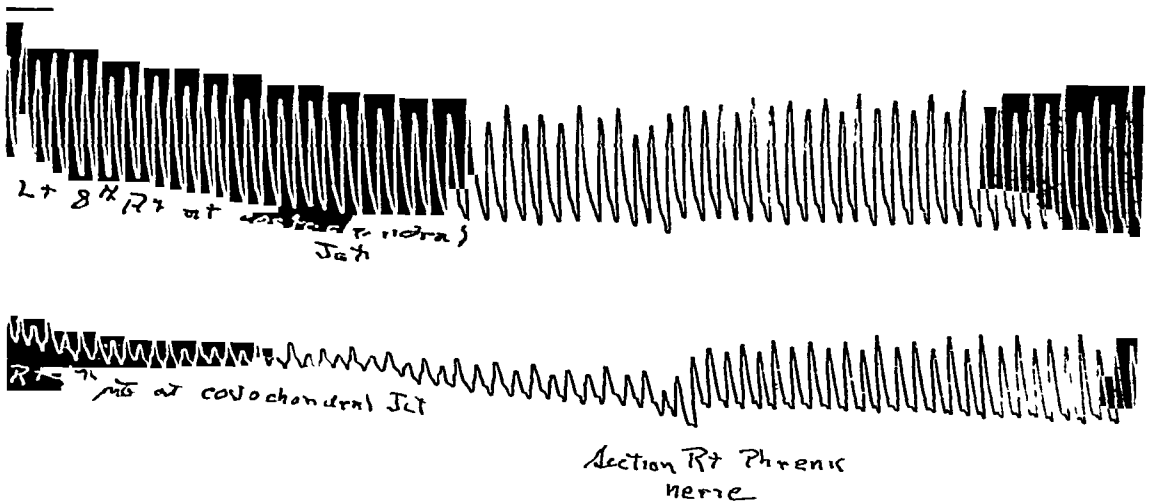
Six months later, the sinus was still present, and examination at this time showed that on inspiration the area of the old wound was drawn forcibly inward and downward, and that there was a paradoxical movement of the ribs of the entire lower thorax. The movement of the upper ribs was markedly restricted. It seemed obvious that these phenomena were caused by the pull of the adherent diaphragm, and that the continuous intermittent tug was a factor in preventing healing of the sinus. For this reason, the left phrenic nerve was extracted. Following the operation, the area of the wound was no longer pulled inward on inspiration, and the movement of the upper ribs was markedly increased. The discharge from the sinus showed a decrease of 50 per cent. The vital capacity, which before the operation had been 1,600 cc., was raised to 1,700 cc.

In this case high adhesions between the diaphragm and the wall of the chest produced a paradoxical movement of the lower thorax. This was reversed by paralyzing the diaphragm, with the result that the vital capacity was increased rather than reduced.

EXPERIMENTAL EVIDENCE

Although Gerhardt and Hoover concluded that high adhesions between the diaphragm and the wall of the chest limited thoracic excursion and although Hoover verified this by observations on dogs the phenomenon had not been recorded graphically. For this reason the following experiment was performed.

PROTOCOL — A male police dog weighing 22 pounds (10 Kg) was given an ether anesthesia. Through an upper abdominal incision the right dome of the diaphragm was sutured to the wall of the chest at the level of the fourth rib in



6-20-29

High Diaphragmatic Adhesions - right

The upper tracing shows the respiratory excursions of the left hemithorax; the lower tracing, those of the right hemithorax which had been restricted by the production of adhesions between the diaphragm and the wall of the chest. At the point X the right phrenic nerve was cut. This was followed immediately by a marked increase in the excursion of this side of the thorax.

the midaxillary line. Three mattress sutures were passed through the diaphragm and the wall of the chest so that the free ends hung on the outside of the body and each suture when tied surrounded a rib. The right phrenic nerve was exposed in the neck and the costochondral junction of the two sixth ribs was laid bare for the attachment of the recording apparatus. Threads were fastened to these two points and carried downward above the dog's body and over pulleys and finally were attached to the muscle levers in such a manner that an upward movement of the ribs would produce an upward movement of the levers and vice versa. The

levers were adjusted to make tracings on a revolving smoked paper. The upper lever recorded the movements of the left side of the thorax, and the lower lever, those of the right side.

A normal tracing was taken (figure), which showed a marked limitation of movement of the hemithorax in which the adhesions had been produced. Following section of the right phrenic nerve, the movement of the ribs on this side was immediately and greatly increased.

#### SUMMARY

Adhesions between the diaphragm and the wall of the chest restrict markedly the respiration of the homolateral lung.

In the presence of such adhesions, induction of paralysis of the hemidiaphragm may so increase the costal movements on that side that the vital capacity is increased rather than decreased.

It is suggested that the presence of such adhesions favors the healing of tuberculous lesions in the lungs and should be considered as a contraindication to the operation of phrenico-exeresis.

# AN OPERATION FOR THE TREATMENT OF SPASMODIC TORTICOLLIS \*

WALTER E DANDY M D

BALTIMORE

It would seem that spasmodic torticollis had run the gauntlet of therapeutic efforts, surgical medical and psychic With one exception the surgical methods have appeared after one or two trials and after an all too brief test of time And with this exception the lack of later reports by the authors is in itself almost adequate evidence that the procedures have ended in failure as indeed they must Again, with this one exception, the surgical procedures have been unilateral Regardless of one's interpretation of the underlying spasmodic contractures, one fact is incontrovertible, i e the disease is never restricted to an isolated muscle or to a single group and never to the muscles of one side

To one not acquainted with the subsequent history of cases of this type, it is indeed difficult to understand why the simple excision of a preponderant, rigid, sternomastoid muscle, which dominates the clinical picture, or better still, the division of the spinal accessory nerve supplying it and the trapezius muscle, will not correct the condition But these efforts have long since been found to do little more than to afford at best a brief respite Soon the muscles on the contralateral side pulled the head just as strongly, and when a similar procedure was carried out there, other muscles quickly produced spasmodic contractures just as severe and unrelenting as the original Attempts of this character were more or less in vogue, though unsuccessful, when Keen,<sup>1</sup> America's pioneer neurologic surgeon realizing the more widespread involvement of the cervical muscles of rotation first (1891) divided on one side the posterior divisions of the first second and third cervical nerves at their points of emergence from the vertebrae It is interesting that Keen's surgical effort was advised by Wier Mitchell from whom a functional basis for spasmodic torticollis would not have been unexpected Taylor<sup>2</sup> (1915) reported unilateral division of the upper four sensory cervical nerves by the first intraspinal attack for this condition His procedure was proposed on the basis of Foerster's

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\* Submitted for publication Dec 31 1929

\* From the Johns Hopkins University and Hospital

1 Keen W W A New Operation for Spasmodic Wry Neck—Namel Division or Excision of the Nerves Supplying the Posterior Rotator Muscles of the Head *Ann Surg* **13** 44 1891

2 Taylor A S in Johnson *Surgical Therapeutics* 1915 vol 1 p 525

treatment in Little's disease by reduction of the incoming sensory stimuli McKenzie<sup>3</sup> (1924) carried the intraspinal divisions of the nerves a step farther, sectioning the upper three motor and sensory nerves and the spinal accessory nerve—all on one side only

In the following year (1925), Finney and Hughson<sup>4</sup> reported the first bilateral operation. It had been used in thirty-one cases over a period of twenty years, twelve patients were cured, sixteen were improved and three were unimproved. Both spinal accessory nerves and the posterior divisions of the upper three cervical nerves on both sides were divided. The former were sectioned alongside the sternomastoid muscles, the latter at the points of emergence from the spinal vertebrae. The operation was, in effect, a bilateral Keen's operation plus division of both spinal accessory nerves. These were the first cases of torticollis in which cure was reported, the reason doubtless being that for the first time a number of nerves had been sectioned bilaterally. Moreover, they were the first cases in which the operative results were adequately tested by time. That cure was not obtained in all cases was due to a number of factors, principally, no doubt, to the individual variations in the extent of involvement of the cervical muscles.

The etiology and pathology of spasmodic torticollis are not known. The explanation of the disease is beset with many theories which it is needless to repeat. None is satisfying. I have nothing to contribute to this phase of torticollis, my only strong conviction is that spasmodic torticollis is undoubtedly of organic and not of functional origin. Certainly in the group which I have observed there has been no greater evidence of a psychogenic background than in any other group of lesions subjected to surgical treatment. This, I am sure, is also Finney's strong impression in his larger series of cases. Even could a functional basis be entertained, certainly no treatment along these lines has offered results at all comparable with those obtained by the operation of Finney and Hughson.

#### AUTHOR'S OPERATION

Greatly impressed by the ultimate results of Finney's long struggle with torticollis, it occurred to me that much the same results could perhaps be obtained more simply and easily by attacking the same nerves centrally, i. e., alongside the spinal cord rather than at the periphery. Seven patients have been operated on by this method. Through a high cervical laminectomy in which the laminae of the upper three vertebrae are removed, the sensory and motor roots of the first, second and third

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3 McKenzie Kenneth G. Intrameningeal Division of the Spinal Accessory and Roots of the Upper Cervical Nerves for the Treatment of Spasmodic Torticollis, *Surg Gynec Obst* 39 5, 1924

4 Finney and Hughson. Spasmodic Torticollis. *Ann Surg* 81 255, 1925

cervical nerves are resected (fig 1) Until recently, both spinal accessory nerves were divided alongside the medulla, and the higher medullary branches were also divided independently with a tiny knife But recently this part of the operation has been discarded because it is not always possible to get the anteriormost filaments It has, therefore seemed better to divide the spinal accessory nerve intraspinally at the level of the foramen magnum only in order to expose better the first cervical motor branch When the operation is concluded, the patient is turned on the back, and through two small incisions in the neck the spinal accessory nerves are exposed and divided, and the central ends are reversed and sutured in this position to avoid regeneration (fig 2) Separate section of the spinal accessory nerves requires only a few moments and is I think much better than intracranial division of these nerves at the jugular foramen as carried out by McKenzie in his unilateral procedure To divide this nerve at the jugular foramen, an extra bony defect of considerable magnitude must be made in the occipital bone

In earlier cases the outcome of function of the sternomastoid and trapezius muscles was awaited, and at a later date the spinal accessory nerves were divided, when necessary, under local anesthesia Although the upper three cervical sensory roots had been sacrificed and the cutaneous sensation abolished, there is usually some pain in exposing the spinal accessory nerves Doubtless this pain is of sympathetic origin It is quite variable, however, in one case there was no sensation throughout the dissection of both nerves, in another there was some but not much pain, and in a third the pain was quite severe throughout In the latter case and two others, the postoperative function of the sternomastoid muscle had persisted on one side only

Intradural division of the sensory and motor nerves is easy to perform and is practically devoid of danger to life or function Loss of function in the affected muscles and in sensation of the skin are absolutely total and permanent, because neither the motor nor the sensory nerves can possibly regenerate

I am not convinced that cutaneous anesthesia is of any value in determining the course of torticollis In one of the earlier cases the fourth, fifth and sixth sensory roots were also sectioned in a longer laminectomy It has appeared necessary to divide the upper three sensory roots in order to have access to the motor roots However, it is quite possible that sufficient retraction of the sensory roots may be obtained to permit sacrifice of the motor roots only An effort will be made to determine the practicability of subsequent cases attaining this end It will doubtless be difficult because the sensory roots are short run transversely and are directly over by the motor roots The first cervical sensory root is variable and probably of little concern

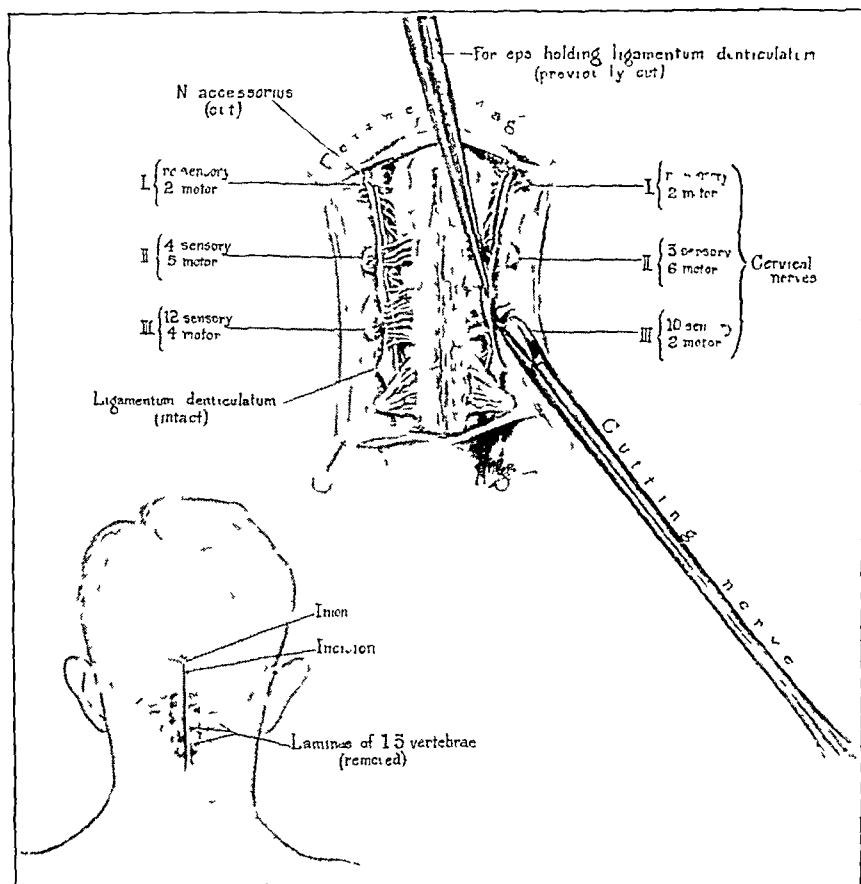


Fig 1—Operative procedure by which the upper three cervical sensory and motor nerves are divided on both sides intraspinally. The instrument shown cutting the nerve was devised by Dr Trimble. It is a combination nerve hook and scissors.

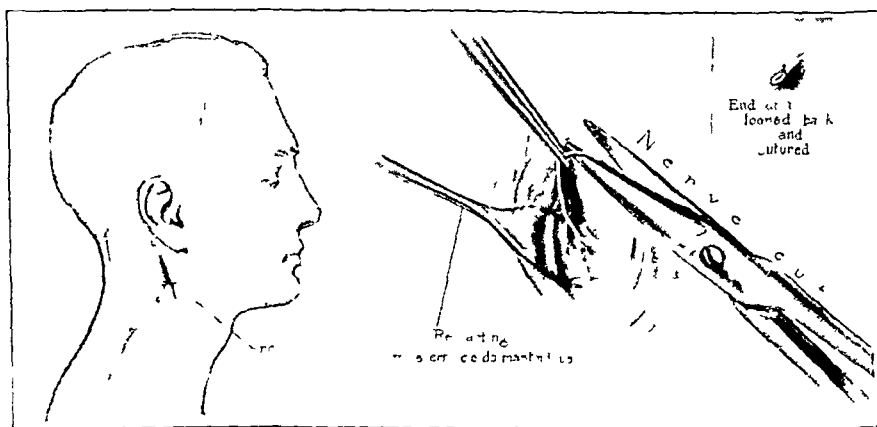


Fig 2—Separate incision used to expose and divide the spinal accessory nerve in the neck on each side. It is sutured in reverse in order to prevent regeneration.

In three of our cases it was absent on both sides and in one case it was present on one side only.

Although the perverted function of chief concern in spasmodic torticollis is rotation of the head and neck there may be associated strong flexion, extension or lateral traction. Practically all of the muscles performing rotation when acting singly also produce flexion or extension when acting together. There are in fact few muscles attached to the head and neck which do not in some degree perform either flexion or extension in addition to rotation or inversely they perform some degree of rotation in addition to the predominant function of flexion or extension. The exact amount of rotation at any time depends on the leverage obtainable by the attachment of the muscle to the head or neck. Muscles such as the longus colli and the scalenus medius are too strictly median to permit of more than a minimal degree of rotation when acting singly. The larger semispinalis capitis (complexus) muscle though mesially placed has such a wide attachment to the skull that when acting singly a fair degree of rotation must result in addition to its predominant function of extension. Even the group of small suprahyoid muscles must play a minor rôle in rotation, flexion and extension of the head and neck.

In looking at the problem of torticollis from an anatomic standpoint, it is therefore, evident that practically all the muscles of the head and neck must be taken into consideration. It is of course, entirely impractical to put them all out of commission in order to obtain a cure. Fortunately this is unnecessary. Finney's proposal which has proved so successful has demonstrated that if the functions of the major rotators are eliminated, in whole or in part the remaining muscles are for all practical purposes adequate to take care of the required movements of the head and neck and by their training subsequent to the operation, the torticollis can be overcome entirely or nearly so. Fortunately, also, the empiric results of Finney and Hughson have shown that it is only necessary to divide the spinal accessory nerves and the upper three cervical motor roots to attain this.

In most cases at first, the head seems a little insecure and lacking in support but this deficit is gradually overcome when the intact or partially preserved muscles are used as a result of training. After a few months scarcely any residual muscular loss can be detected subjectively or objectively. A glance at the accompanying table will show exactly how far the removal of this nerve supply affects these muscles. The function of the entire group of small muscles between the occiput atlas and axis is entirely abolished. The remaining muscles are entered in their probable importance as rotators of the head and neck. It will be seen that some of the larger muscles retain part—even a large part—of their nerve supply after the operation and therefore function in restricted degree. Of the more important muscles of rotation only



the functions of the sternomastoid and trapezius and splenius cervicis, the longissimus capitis and cervicis, the semispinalis capitis and the levator angulae scapulae and the group of scaleni muscles are affected only in part

*Muscles Involved in Torticollis*

Group I	Muscles	Nerve Supply	Function After Operation
Small muscles between the atlas axis and the occiput	Rectus capitis anterior	First and second cervicals	Abolished
	Rectus capitis lateralis		
	Rectus capitis posterior major		
	Rectus capitis posterior minor		
	Obliquus capitis inferior		
Group II  Larger muscles of neck (arranged in order of importance)	Sternomastoid	Spinal accessory second and third cervicals	Abolished
	Trapezius	Spinal accessory second and third cervicals	Abolished
	Splenius capitis	Second and third cervicals	Abolished
	Splenius cervicis	Fourth to eighth cervicals	Unaffected
	Levator anguli scapulae	Third and fourth cervicals	Only partially lost
	Longissimus capitis	Second to fifth cervicals	Partially lost
	Longissimus cervicis	Fifth to eighth cervicals	Unaffected
	Semispinalis capitis (Complexus)	Second to eighth cervicals	Partially lost
	Longus capitis	First, second and third cervicals	Abolished
	Scalenus anterior	Second to seventh cervicals	Slightly affected
	Scalenus medius		
	Scalenus posterior		
Group III  Muscles of deglutition, many of which play a minor role in rotation of the head and some are affected by section of the cervical nerves	Digastric	Fifth and seventh cranials	Unaffected
	Stylohyoid	Seventh cranial	Unaffected
	Mylohyoid	Fifth cranial	Unaffected
	Geniohyoid	Twelfth cranial	Unaffected
	Geniohyoglossus	Twelfth cranial	Unaffected
	Hyoglossus	Twelfth cranial	Unaffected
	Thyrohyoid	Twelfth cranial	Unaffected
	Sternohyoid	First, second and third cervicals and twelfth cranial	Affected
	Omohyoid	First, second and third cervicals and twelfth cranial	Affected
	Sternothyroid	First, second and third cervicals and cranial	Affected

The retention of muscular function obviously explains the failure to obtain complete cure in all cases of torticollis, in some cases the result has fallen just short of complete cure and in practically all tremendous improvement has been secured. This statement is based on the results in the cases of Finney and Hughson and my own.

The limits of intraspinal section of the cervical nerves are reached by the operation here reported. Since the fourth cervical nerves give

rise to the phrenic nerves and the remaining cervical nerves to the branchial plexus they must be left intact. In those more refractory cases which retain some degree of imperfection after operation, it is possible to pick out more readily a single or small group of offending muscles and remove their nerve supply by a minor peripheral operation. In one of my cases the head is entirely quieted, but the levator angulae scapulae muscle continues to act. As this muscle receives its nerve supply from the third and fourth cervical nerves, its function is partly retained after the intraspinal operation. Improvement should be anticipated by peripheral division of the branch of the dorsalis scapulae nerve.

#### REPORT OF CASES

*Group 1 Cases in Which Cure is Reported*—CASE 1—A physician, aged 40, four years before being operated on for spasmodic torticollis, experienced a slight aching pain in the lower cervical vertebrae, which tended to be transmitted around both sides of the neck. At that time, she paid little attention to it. During this attack, the head began to draw to the right and backward, both steadily and spasmodically. Relief was obtained by allowing the head to hang over the edge of the bed. Over a period of two years, the symptoms gradually disappeared—the shaking first, the pain later. For a year and a half, she was quite well. Four months before operation, the head again began to draw to the left instead of to the right, as in the first attack. This state of powerful contraction of the rotator muscles persisted without signs of relenting. If the head was forcibly drawn to the other side, it returned in a few seconds. At times, there was numbness in both arms. Until two months before, there was a sore spot at the base of the neck on the left side.

*Examination*—Aside from the local condition, there were no objective signs. The head was strongly drawn to the left and slightly backward. The sterno-mastoid muscles seemed to preponderate.

*Operation*—April 11, 1928. The spinal accessory, the first, second and third motor roots and the upper five sensory roots (the first sensory root was absent on both sides) were sectioned intraspinally.

Subsequent division of the left spinal accessory nerve in the neck was necessary in this case.

*Result*—After operation, there were minor jerkings of the head. These were gradually overcome during the next few months. Since then, the patient has been free from symptoms.

CASE 2—An army officer, aged 40, had torticollis, with turning of the head to the left, for the past two years. Previous to the onset of this trouble, he had had two or three attacks of "crick in the neck" each year. Sixteen years before, one of these attacks kept him bedfast for several days, four years before another equally severe attack was followed three days later by an excruciating "neuritis" in the left arm lasting for a month. Throughout the duration of the torticollis, the head had drawn steadily to the left. He could counteract it only by holding the hand on the head. There were no spasms. The examination revealed nothing except the local condition. The head was drawn strongly to the left, efforts to correct this position caused the head to jerk. The left sterno-mastoid muscle was drawn like a tight cord across the neck.

*Operation*—Nov 26, 1928 Laminectomy of the upper three cervical vertebrae was performed. The spinal accessory nerves and the upper three cervical motor and sensory nerves on both sides were sectioned intradurally. Subsequent division of the spinal accessory nerves in the neck was unnecessary.

*Result*—Immediately after the operation, the same tendency to draw the head to the left was evident at times, there was also some unsteadiness of the head. The patient spent several months abroad and returned free from all symptoms and has so remained to date. He has resumed his occupation.

*CASE 3*—An accountant, aged 47, had been troubled with a stiff neck for eight years. One year earlier (nine years before operation), a dull pain persisted along the right side of the neck for several months, finally disappearing. One year before, his head began to draw to the right. Six months before, the head began to draw to the left and the left shoulder began to elevate.

The results of the examination were negative, except for the outspoken torticollis with rotation to the left.

*Operation*—March 20, 1929 Cervical laminectomy was performed. The spinal accessory and the first, second and third sensory and motor roots on both sides were sectioned intradurally. Before the patient left the hospital, the left spinal accessory nerve was divided in the neck.

*Result*—Unsteadiness of the head persisted in slight degree for two or three months, gradually abating. Immediately after operation, the patient complained of some subjective difficulty in swallowing, but aside from some tardiness there was no objective evidence of dysphagia. There has since been improvement but not entire correction.

*CASE 4*—A sparsely nourished woman, aged 61, presented a most remarkable picture of torticollis. When lying in bed, her head was quiet and could be maintained in any position, but immediately on assuming a sitting posture her head would snap with great violence. Although the most common direction of the sudden thrust of the head was to the right, it was frequently to the left, at other times, backward and forward. She was never able to swallow when sitting or standing unless the head was strongly supported. With the head at rest in the recumbent position, there was no dysphagia. She dated her trouble to a so-called nervous breakdown five years before. She had been weak and nervous and unable to carry on any longer. Two months later, pain and jerking appeared in the neck. It was intermittent at first, but recently had become incessant when she was not in a recumbent position.

*Operation*—Oct 31, 1929 Tribromethylalcohol anesthesia was administered by rectum. Both spinal accessory nerves and the first, second and third sensory and motor nerves on both sides were sectioned intraspinaly. Two weeks later, both spinal accessory nerves were divided without any anesthesia and absolutely without pain, except when the spinal accessory nerves were handled. This pain was referred to the ear and angle of the jaw.

*Result*—The patient remained in the hospital one month. She was practically devoid of involuntary movements of the head or neck at all times after the operation.

*CASE 5*—A fairly well nourished man, aged 59, referred the onset of his trouble to a spell of constant pressure and stiffness in the back of the neck. This occurred four years before operation for torticollis, lasted six months and disappeared completely. Soon thereafter, sudden attacks of intermittent spasms of the muscles of the neck caused rotation of the head to the right every two or three minutes. Gradually the attacks fused and strong rotation of the head

persisted to the right. Shortly after the onset of his trouble, he had difficulty in swallowing. This became so severe that he could scarcely take any nourishment, and in two weeks he lost 20 pounds (9 Kg). Without apparent reason, swallowing gradually improved and finally became normal. It was, however, always necessary to steady the head with his hand in order to permit swallowing. The contractions were said to cease during sleep, but the rotation of the head to the right persisted. The platysma contracted during the attacks, and athetoid-like movements of the hands and arms participated.

*Operation*—April 20, 1925. The spinal accessory, first, second and third cervical and sensory nerves on both sides were sectioned intradurally.

This was one of the most severe cases of the series. Three months before this operation, the patient had been operated on by Dr. Finney. He seemed so little improved that at Dr. Finney's suggestion I cut the nerves intradurally for the first time. On discharge from the hospital three weeks later, the patient was considerably improved though far from well. I have not seen him since then and was fully prepared to be told, in response to an inquiry, that he was still affected. The following excerpts from his letter (Dec. 1, 1929), however, lead me to include him with the patients cured: 'I have been doing very well. My neck does not pull or jerk any more. I weigh 143 lbs., the best I ever weighed was 153.'

This case well emphasizes the importance of time and practice in overcoming the traces of the malady which still linger after the operation. I am, therefore, not at all sure that the same results might not well have followed Dr. Finney's operation had he been given the advantage of the same period of time for recovery.

*Group 2. Cases in Which Great Improvement but Not Cure Is Reported*—  
CASE 6—A school teacher, aged 41, had severe tension of the head to the left and downward. Although the head was always strongly rotated, there were frequent superimposed spasms. Voluntary efforts increased the unsteadiness of the head. She dated her trouble to a "nervous strain" a year before. Soon thereafter, the head began pulling to the left. Recently, the character of the attacks changed. The head drew to the right and backward. A rest cure of eight weeks seemed to bring some improvement, but it was slight and very transient. A brace between the head and shoulders was worn for two weeks without appreciable benefit. Contractions were worse when she was lying down. Her voice was greatly affected for some time, and she was able to talk only in a whisper for several weeks.

*Operation*—Nov. 14, 1928. Both spinal accessory, the first, second and third cervical sensory and the motor roots on both sides were sectioned intradurally. Three months later, with the patient under local anesthesia the right spinal accessory nerve was divided in the neck. Although the skin was anesthetic from the loss of sensory nerves, it was necessary to use procaine hydrochloride freely in the deeper approach to the spinal accessory nerve. Section of this nerve produced a sharp deep pain in the ear and at the angle of the lower jaw.

*Result*—The head is perfectly still but the neck continues to draw to the left and to rotate slightly. The muscle involved is undoubtedly the levator anguli scapulae, perhaps the scaleni are also involved. The end-result of this strong muscular pull is a curvature of the neck. The patient has subconsciously overcome the curvature by a counter pull and holds the head erect without conscious effort. She feels so well that she is unwilling for the present at least to have

the nerve to the levator anguli scapulae muscle divided in the neck. She is again teaching school. Her voice, though still not normal, is greatly improved and carries without apparent effort.

**CASE 7**—A sparely nourished man, aged 54, a bookkeeper and accountant, first noticed jerking of the right shoulder upward and forward when writing two years before operation. Sixteen months before, his head drew downward and to the right, remaining there all day. A few days later this contraction was repeated, and since that time the head had remained almost constantly down in that position when the patient sat or stood. Partial relaxation occurred when he was in a recumbent position. Jerking developed only when he attempted to correct the position of the head. Relief was obtained when his mind was diverted, it was intensified by nervous strain.

**Operation**—Oct 9, 1928. The spinal accessory, first, second and third cervical sensory and motor roots on both sides were sectioned intradurally. Ten days later, with the patient under local anesthesia, the right spinal accessory nerve was divided in the neck.

**Result**—This is the only case in the series in which unsatisfactory results were obtained. Objectively, the patient is tremendously improved, certainly more than the patient in the preceding case. Indeed, with very little effort on his part, the slight rotation which exists could easily be overcome by voluntary effort. He is the only psychoneurotic patient of the series. His chief complaints now are sensory rather than motor, the most serious trouble being a sensation of a steel bar that is constantly separating his shoulders and holding them apart. Pains were constantly present in the neck and head. Being most introspective, he is continually striving to find an underlying cause for his symptoms, experimenting with medicines and seeking the advice of numerous physicians. A background of serious family and financial troubles has added greatly to the somatic psychosis. He cannot be induced to make any effort to readjust himself to his family or to renew his work.

#### RESULTS OF THE OPERATION

Of the eight patients included in this effort, five appear to be practically cured, two fall short of a complete cure but are greatly improved, the remaining one is not living. In four of the cases in which cure has been recorded, the patients have been personally examined from time to time since the operation. The lapse of time since the operation is twenty, fourteen, nine and two months. These patients have consistently improved since the operation, and without exception have had no recessions. All patients, with the exception of the one operated on recently, have returned to work. Perhaps it is not justifiable to include the last case in which only two months have elapsed since operation. My reasons for doing so are that this case was the most severe in the group, and the patient was more perfectly relieved immediately after the operation than any of the others. The fifth patient considered as cured has not been seen since the operation. The inclusion of this case in the group in which cure was obtained is based on the patient's letter in which he stated that his head no longer jerks and draws. He was the first patient operated on by this method.

The two patients who were not completely cured are greatly improved. Perhaps a conservative estimate of the improvement in these patients whom I have observed from time to time, would be about 85 per cent. The degree of objective improvement is about the same in each instance and in each the levator anguli scapulae muscles (possibly the scaleni are partly at fault) seem to be the cause of failure to obtain complete cure.

There has been no operative mortality in the series. The single death occurred three weeks after operation and was due to pneumothorax contracted ten days after the operation. During the first ten days the patient was entirely free from fever—a fact which eliminates the anesthetic as the cause. He was a very bad surgical risk having auricular fibrillation and advanced myocarditis but he was so miserable that we were prevailed on to accede to his urgent wish for the operation.

In only one instance has there been entire freedom from minor jerking or drawing of the head immediately after the operation. The movements, however, lack the tremendous force of the preoperative state. Nevertheless, the mere existence of the same muscular effects after the operation will have a severe psychologic effect on patient and surgeon alike if its existence and import are not realized. The patient should be prepared in advance to know that the resultant cure will not be instantaneous. After convalescence from the operation, the patient should be induced if possible, to spend from three to six months in rest and in graduated exercises which will strengthen the muscles of the neck. Finney and Hughson emphasized the importance of the postoperative period of training in eliminating the last traces of muscular incoordination.

Mention should be made of a minor degree of dysphagia which was noticed in two of my patients. It is noticed principally in swallowing solids. The act of deglutition is always possible but more effort is required. Since dysphagia was not present before operation, it must be due to loss of the nerve supply to some muscle of deglutition. But since this disturbance was absent in five cases, one is led to wonder whether the muscles involved may not have a variable nerve supply. The table (group III) showing the muscles involved in deglutition and their nerve supply indicates that three of the infrahyoid muscles—sternohyoid, sternothyroid and omohyoid—partially lose their nerve supply by the operation. Each of these muscles also receives a partial nerve supply from the hypoglossal nerve i. e. through the ansa hypoglossi and this remains intact. The remaining infrahyoid muscle—the thyrohyoid—is supplied exclusively by the hypoglossal nerve. The partial loss of the infrahyoid muscles leaves the many suprahyoid muscles, to a degree unopposed. The varying degree of nerve supply to the

infrahyoid muscle, i. e. whether from the cervical or the hypoglossal nerves, probably explains the difference in results with respect to deglutition

#### DIFFERENCE BETWEEN THE AUTHOR'S OPERATION AND THAT OF FINNEY AND HUGHSON

In the operation of Finney and Hughson, only the posterior divisions of the first three cervical nerves are divided, the anterior divisions being inaccessible. By their operation, therefore, the following muscles of rotation remain intact or in part as indicated: (1) rectus capitis lateralis, (2) rectus capitis anterior, (3) longus capitis, (4) sternomastoid (branches from the second and third cervicals), (5) trapezius (branch from the third cervical), (6) levator anguli scapulae (branch from the third cervical).

I am not sure that the muscles retained by their operation and sacrificed by mine will eventually make any difference in the ultimate result. It is my impression that the principal difference, if any, would lie in the partial preservation of function in the more powerful muscles, i. e., the sternomastoid, trapezius and levator anguli scapulae muscles.

#### SUMMARY AND CONCLUSIONS

1. An operative procedure is presented for treatment in spasmodic torticollis. The first, second and third sensory and motor roots on both sides are sectioned intradurally, and the spinal accessory nerves are divided peripherally, small incisions in the neck being used.

2. Eight patients have been operated on by this method with the following results: (a) five appear to be cured, (b) two are greatly improved but not cured, (c) one died of pneumonia (not contracted at the time of operation) three weeks after operation.

3. Torticollis is cured by removing the nerve supply from the major muscles of rotation. The remaining muscles will overcome in time and by training the lost motor function and in most instances any remaining traces of the condition.

NOTE.—Since this article was submitted for publication I have sectioned the upper three motor cervical nerves on both sides without sacrificing any sensory fibers. There was no difficulty in avoiding the sensory roots, and the preservation of sensation should make a worthwhile improvement in the procedure.

# FORTY-FIRST REPORT OF PROGRESS IN ORTHOPEDIC SURGERY\*

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## CONGENITAL DEFORMITIES

*Torticollis*—Von Lackum<sup>1</sup> advocated early operative treatment for torticollis and reported four cases in infants ranging in age from 5 weeks to 5 months in whom the scar of the belly of the sternomastoid was excised. None of the cases had responded to manipulative measures. The injury was found to be sharply limited within the sheath of the sternocleidomastoid muscle. No attempt was made to suture the ends of the muscle after excision of the scar.

*Cleidocranial Dysostosis*—Fitchet<sup>2</sup> reported eight additional cases of this anomaly, six of which occurred in three generations of one family. The article furnishes an excellent review of the literature.

*Congenital Dislocation of the Hip*—Putti<sup>3</sup> made a plea for earlier treatment in congenital dislocation of the hip. In certain parts of Italy,

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\*Submitted for publication May 5 1930

\*This report is based on a review of 315 articles selected from 808 titles dealing with orthopedic surgery appearing in medical literature between June 1 1929 and Nov 30 1929. Only those papers which seem to represent progress have been selected for note and comment.

1 Von Lackum H L. *Surg Gynec Obst* 48 691 (May) 1929

2 Fitchet S M. *J Bone & Joint Surg* 11 838 (Oct) 1929

3 Putti V. *J Bone & Joint Surg* 11 798 (Oct) 1929



through educational propaganda people bring their small children for examination on the slightest suggestion of an abnormality. In this way, many congenital dislocations are recognized during the first year. The roentgenogram at this age will show the nucleus of the upper femoral epiphysis absent or smaller on the dislocated side, the top of the femur some distance from the floor of the acetabulum and higher than normal and an increase in the slope of the acetabulum. If the legs of these small children are kept in a position which compels the femoral heads to exert pressure on the acetabula for several months, reduction of the dislocation and normal development of the joint will usually occur. The author devised a triangular wooden frame adjustable to different angles. To this the child's legs are strapped in the maximum amount of abduction and internal rotation. The frame is removed for bathing and manipulations in abduction and internal rotation. X-ray pictures are taken every two months. Treatment is discontinued when reduction is perfect and the reconstruction of the joint well advanced. Treatment usually lasts from eight to twelve months.

#### NUTRITIONAL AND METABOLIC DISTURBANCES OF BONE

*Vioosterol*—Smith and Elvove,<sup>4</sup> studying the effects of vioosterol in rabbits, found doses of 2 mg or more usually fatal, autopsy showing calcification of the aorta, kidney and lung. Smaller doses increased the blood serum calcium rapidly, and a moderate increase in the inorganic phosphates of the serum was observed.

Hess, Lewis and Rivkin<sup>5</sup> stated the belief that vioosterol is a specific for rickets, tetany and osteomalacia. A standard dose has been established for the prevention and cure of rickets. Premature and exceptionally rapid growing infants must be regarded as a separate group, and dosage should be based on a biologic estimation of antirachitic potency rather than a gravimetric assay of the vioosterol. Such products should be subjected to careful laboratory control.

An editorial<sup>6</sup> after pointing out the potency of this drug, quoted the warning of the United States Public Health investigators: "Of course we would not be understood as deprecating the therapeutic use of irradiated ergosterol, but would rather call attention to the possible harm that might result from too large doses."

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4 Smith, M. I., and Elvove, E. Pub Health Rep **44** 1245 (May 24) 1929

5 Hess, A. F., Lewis, J. M., and Rivkin, H. Status of Therapeutics of Irradiated Ergosterol J A M A **93** 661 (Aug 31) 1929

6 Irradiated Ergosterol—A Reminder editorial, J A M A **92** 2023 (June 15) 1929

*Parathyroids*—Richardson, Aub and Bauer<sup>7</sup> reported a case of apparent osteomalacia with aseptic cavities throughout the bones suggestive of osteitis fibrosa. The patient was a man aged 34, who presented marked muscular weakness, gave a history of multiple fractures and presented x-ray pictures showing marked diminution of calcium throughout the skeleton. Studies of the calcium and phosphorus revealed (1) markedly elevated serum calcium, (2) greatly increased calcium secretion, (3) reduced serum phosphorus and (4) increased phosphorus excretion. By removal of the parathyroid glands the patient was greatly benefited. His muscle tone improved, there was a greater increase in calcium deposit in the bones. He sustained no further fractures and was able to return to work. A review of the work on parathyroidectomy in conditions of calcium deficiency in bones is appended.

*Experimental Acromegaly*—Teel and Watkins<sup>8</sup> noted a marked drop in the nonprotein nitrogen of the blood of dogs after injection of pituitary anterior lobe extract. They said that this effect may be one of mobilizing protein from the blood for the purpose of building up new protoplasm. This is in harmony with the pronounced rapidity with which many of the tissues and organs grow during acromegaly.

*Osteitis Deformans*—Bascourret and Decourt<sup>9</sup> studying ten cases of Paget's disease found in each case comparing the affected and the nonaffected limbs differences suggesting changes in the sympathetic nervous system, increased local temperature, hyperpulsatility of the arteries, etc. From this they argued that the bony changes are due to disturbances in the trophic nerves particularly the tractus intermedio-lateralis as in tabes.

#### SCOLIOSIS

In ankylosing the spine for scoliosis Kleinberg<sup>10</sup> would employ as much as possible of the Hibbs technic but would add the massive tibial graft of Albee, placing it on the concave side. With a marked razor-back deformity, resection of a portion of the involved ribs and the use of such ribs for a graft in fusion is a valuable procedure. Selection of the portion of the spine to be fused is important and an attempt should be made to select the primary curve. At any rate the dominant curve or the more deformed curve should be the one of choice. Ninety patients have been operated on by Kleinberg since 1919. The results in fifty-four of the cases are recorded. Forty-two or 78 per cent obtained excel-

7 Richardson, E. P., Aub, J. C. and Bauer, W. *Ann Surg* **90** 730 (Oct) 1929.

8 Experimental Acromegaly, editorial *J. A. M. A.* **93** 849 (Sept 14) 1929.

9 Bascourret, M. and Decourt, J. *Rev. Neurol.* **36** 606 (April) 1929.

10 Kleinberg, S. *J. Bone & Joint Surg.* **11** 66 (Jan) 1929.

lent results, i e., arrest of deformity, satisfactory appearance of the back and relief from backache, 13 per cent had good results, i e., good appearance of the back but slight or doubtful increase in the curve, 9 per cent were failures, i e., there was a distinct increase in the deformity

#### PAIN IN THE BACK, SCIATIC PAIN AND SPONDYLITIS

*Lumbosacral Deformities*—A study of 3,000 radiograms formed the basis for this essay for which Brailsford<sup>11</sup> received the Robert Jones medal and the British Orthopaedic Association's prize for 1927. The deformities in this area of the spine are grouped by Brailsford under the following headings: (1) congenital abnormalities, (2) injury, (3) inflammation, (4) neoplasms and (5) disease of bone of uncertain origin.

Congenital abnormalities were present in 26 per cent, often giving rise to no symptoms or signs, and detectable only by roentgen examination. The most frequent deformity associated with developmental irregularity was scoliosis due to asymmetrical sacralization of the fifth lumbar vertebra. Sacralization of the fifth lumbar vertebra was found in 8.1 per cent (3.4 per cent unilateral, 4.7 per cent bilateral) of the cases. Ossification of the lumbolumbar ligaments might occur and was usually associated with pain. Arthritic changes and osteophytic outgrowths encroaching on the nerve foramina were often present in irregular and asymmetrical joints. The articular facets of the fifth lumbar were directed in many ways—57 per cent backward, 12 per cent inward, and in 31 per cent mixed, facing in different directions on the two sides.

Five examples of spondylolisthesis were found in the series. Brailsford expressed the belief that this condition is frequently erroneously diagnosed, and he expressed doubt concerning the possibility of manipulative reduction. Both anteroposterior and lateral views are needed for one to be certain of the diagnosis, either by itself may mislead. None of the five patients complained of pain in the back, and in four there was no pain. The gait of two was normal, of two it was waddling, and the fifth had a marked limp. With regard to injury, severe trauma can occur in the lumbosacral region without producing a spondylolisthesis. Lipping of the margins of the vertebral bodies and calcification of the connecting ligaments were occasionally seen as a sequel of an injury which had apparently not caused any bony damage. Fracture of a transverse process might easily be erroneously diagnosed from the roentgenogram. In osteo-arthritis lipping of the border of the bodies was common but Brailsford, contrary to Putti, concluded that the articular surfaces were usually smooth and presented no irregularities. Spondylolisthesis was not a common sequel of tuberculosis of the lumbosacral

11 Brailsford J. F. Brit J Surg 16:562 (April) 1929.

region on the contrary the lumbar lordosis was usually lost the sacrum flat and the lumbosacral angle obliterated. Two examples of gummas of the vertebrae were noted. Brulstord relied for the diagnosis on the large amount of symptomless destruction with sclerosis and on the overgrowth of the bone around.

[**ED. NOTE**—In the interpretation of roentgenograms of the lumbosacral region this paper is valuable as a reference. An extensive bibliography is given.]

Hibbs and Swift<sup>12</sup> reported their results in 150 cases of lumbosacral fusion in the majority of which one of the following conditions was present: (1) an unusually acute lumbosacral junction, (2) spondylolisthesis, (3) sacralization of one or both transverse processes and (4) incomplete fusion between the first and the second sacral vertebrae. They stated that 73.3 per cent of their patients were entirely relieved, 14 per cent were improved and 12.7 per cent were unimproved.

Mueller<sup>13</sup> demonstrated several cases of spondylolisthesis which, according to the patients, have been caused by traumatism. He said that he regards this as incorrect, claiming that the condition is congenital in nature or exists from early youth. From a study of x-ray pictures, the inclination of the sacrum averaged 67.5 degrees in persons standing. This however had nothing to do with the development of spondylolisthesis. Children with bilateral congenital dislocation of the hips often had a certain degree of spondylolisthesis.

Ayers<sup>14</sup> expressed the belief that the cause of pain in the lower part of the back with sciatica is a disturbance at the lumbosacral junction and not in the sacro-iliac region. His analysis of the anatomic distribution of pain in these cases (buttock, posterolateral thigh and calf and outer side of ankle) is that it is distributed along the course of the fourth and fifth lumbar and first sacral nerves which he stated do not come in relation to the sacro-iliac joints. He also stressed the observation of Wilson and Danforth that the fifth lumbar nerve root while being the largest lumbar branch, has the smallest exit from the vertebral canal. Many of the x-ray pictures in his cases showed an arthritis of the facets at the lumbosacral junction, a thinning of the cartilage or rarely, spondylolisthesis. For treatment in this condition he advised immobilization by the Hibbs method of fusion. Thirty-six cases in which fusion was done are reported.

*Arthritis*—Gunther and Sampson<sup>15</sup> stated the belief that precordial pain from osteo-arthritis of the spine is distinguished by its close relation

12 Hibbs R. A. and Swift W. E. *Surg. Gynec. Obst.* **48**: 604 (May) 1929.

13 Mueller, W. *Zentralbl. f. Chir.* **57**: 234 1930.

14 Ayers C. E. *New England J. Med.* **200**: 592 (March 21) 1929.

15 Gunther L. and Sampson J. J. *Radicular Syndrome in Hypertrophic Osteoarthritis of Spine*. *J. A. M. A.* **93**: 514 (Aug. 17) 1929.

to motion of the spine and that relief is afforded by mechanical appliances and a nonresistant surface for sleeping. Associated sensory changes are often present. This type of pain does not respond to vasodilators.

#### TUBERCULOSIS

*Potts' Disease*—Sorrel<sup>16</sup> resumed the results of his researches on the mechanism, the signs and the prognosis in Potts' paraplegia. If one eliminates the paraplegias from osseous compressions which are exceptional, one may consider two varieties of paraplegia, that caused by abscess and that caused by pachymeningitis. The paraplegias caused by abscess occur early, usually toward the end of the first year, and rapidly become complete. They have a tendency toward spontaneous regression in 90 per cent of the cases. They are by far the more frequent. The paraplegias caused by pachymeningitis are late, often occurring in old cases of Potts' disease which are irregularly healed. They develop slowly, often remaining incomplete, and while they seem less grave, they are more severe, having no tendency toward regression. Sorrel's opinion is that any surgical treatment, spinal graft or laminectomy can influence to an appreciable degree the natural evolution of these paraplegias, favorable in the first type and unfavorable in the second.

[ED. NOTE—This is an excellent summary of the situation and well worth quoting to all students.]

*Tuberculosis of the Joints*—Girdlestone<sup>17</sup> stated his indications for open operation, as part of the treatment, in tuberculosis of the larger joints. In adults, operation should be the rule as soon as the general condition of the patient is on the mend. In children, operation is indicated whenever sufficient damage has been done to the joint to make movement incompatible with permanent safety from relapse, but the operation should not be undertaken until after one year of nonoperative treatment and not before the child has reached the age of 10. The type of operation advocated varies with the different joints: for sacro-iliac disease, Verrall's extra-articular arthrodesis, for disease of the hip, extra-articular arthrodesis, with excision in addition when massive granulation tissue is present, for tuberculosis of the knee, partial excision and arthrodesis, for tuberculosis of the shoulder, excision and arthrodesis. This author does not favor operations on the elbow, and is doubtful about the advisability of operating on the ankle. Amputation is indicated in many patients beyond middle age. For secondarily infected joints, he advocates the preliminary removal of sepsis by wide drainage opera-

16 Sorrel E. Bull. et mem. Soc. nat. de chir. de Paris 55:658 (May 18)

17 Girdlestone, G. R. Brit. M. J. 2:529 (Sept. 21) 1929

tions. Gardlestone emphasizes the fact that operation is not a substitute for but an adjunct to nonoperative treatment.

*Tuberculosis of the Hip*—Pattison<sup>18</sup> recorded the immediate results in 300 cases of tuberculosis of the hip joint. The diagnosis was made by clinical observation but care was taken to exclude all cases in which the patients were suffering from some obvious condition such as cox vara, pseudocoxalgia or pyogenic arthritis. Also all cases of transient arthritis in which the condition cleared up within a month were excluded. His results were as follows: (1) cured (perfect movement, no shortening, no sign of disease) 167 or 55 per cent, (2) arrested (diminution of movement, shortening, deformity) 97 or 32 per cent, (3) relapse 28 or 9 per cent, and (4) dead or dying 13 or 4 per cent.

[Ed. NOTE—Pattison is working at a county hospital and treats his patients with recumbency and traction. But we do not believe any one will accept the statement that all of the 55 per cent of patients who were cured had suffered from tuberculous disease of the hip.]

*Tuberculosis of the Knee*—Pouzet,<sup>19</sup> in the service of Professor Nove-Josserand, studied juxta-articular tuberculosis in twenty-five old cases in children, of these thirteen had femoral and twelve tibial lesions. He came to the following conclusions: 1. Such lesions may heal by conservative measures but the treatment is long and the results uncertain. 2. By excising these lesions the duration of treatment is reduced two-thirds, and the removal of the focus renders the cure more certain. It is necessary always to immobilize after the operation until the cure is complete. 3. The indications for the operation depend on the age (before 5 or 6 years), the possibility of surrounding the lesion and the condition of the joint. 4. As to the disturbance in growth, the author stated that this is due to the destruction of the epiphyseal cartilage and does not depend on the method of treatment.

Lance<sup>20</sup> discussed the use of a bone graft of the knee after the manner of Lexer. It consists of a transfexion by an autogenous graft without actually opening the joint. The principal indication according to the author, is the incomplete and painful ankylosis which follows a tuberculosis of the knee in childhood. It is less mutilating than a resection at the same time acting as an arthrodesis. It should be used in cases in which there is shortening. If there is shortening, the fixation should be in extension, if there is no shortening it should be ankylosed in some flexion. In active cases the danger of establishing a sinus is overbalanced by the advantages of the operation. In the author's cases how-

18. Pattison, C. L. Brit. M. J. 2: 532 (Sept. 21) 1929.

19. Pouzet, F. Rev. d'orthop. 16: 297 (July) 1929.

20. Lance, M. Bull. et mem. Soc. nat. de chir. de Paris 55: 625 (May 11) 1929.

ever, the patients did not do so well when there was activity. He therefore regards the procedure as more suitable for old inactive but painful cases.

[ED NOTE—Pouzet's procedure may be sound for small foci, but we doubt the possibility of successfully excising tuberculous foci when we must depend on the x-ray picture to determine the extent of such foci. In our experience, the disease may have spread so far beyond the apparent focus that definite limits can not be found. With the method described by Lance, we have no experience. Erasion or fusion operations seem to offer a more certain means of obtaining satisfactory fixation.]

#### POLIOMYELITIS

Aycock,<sup>21</sup> in a study of the seasonal and climatic fluctuations in the incidence of infection from poliomyelitis, reached the conclusion that these fluctuations are due to changes in the resistance of the subject. He does not consider the dose or the virulence of the virus as important factors. As evidence for postulating such geographic and seasonal variations in the subject's resistance or "autarcesis," as he terms it, the author cited seasonal variations in growth and changes in weight of various organs with different seasons and climates. Such changes, in his opinion, produce a physiologic imbalance, making the subject less resistant to the virus.

Aycock and others<sup>22</sup> reported the results of treatment with convalescent serum in 116 cases of preparalytic poliomyelitis in Massachusetts during 1928. The results were more carefully controlled than in the patients treated at Haverhill, Mass., in 1927. A striking decrease is shown in the mortality and amount of paralysis in the treated patients as contrasted with the untreated ones. This cannot be measured readily in percentages.

McEachern<sup>23</sup> and his co-workers reported their results in administering poliomyelitis convalescent serum during the Manitoba epidemic in 1928, seventy-four of 161 patients received this serum. Fifty-four received no serum and thirty-three received it after the onset of paralysis. Of fifty-seven patients receiving an average of 25 cc. of the serum intramuscularly in the preparalytic state, 93 per cent recovered, and there were no deaths. Of the fifty-four patients receiving no serum, 26 per cent recovered, 11 per cent died and the remainder were paralyzed. They

21 Aycock, W. L. *J. Prev. Med.* **3**: 245 (May) 1929.

22 Aycock, W. L., et al. *Preparalytic Poliomyelitis*, *J. Infect. Dis.* **45**: 175 (Sept.) 1929.

23 McEachern, I. M., et al. *Canad. M. A. J.* **20**: 368 (April) 1929.

concluded that convalescent serum was of value while the prodromatic stage and that the intramuscular route is efficacious.

Divelev<sup>24</sup> studied 182 cases of poliomyelitis developing during an epidemic in Kansas. Eighty-five of the cases were carefully followed by the author for two years. He concluded that by early drainage of the spinal canal and intravenous or intramuscular administration of immunized horse serum or better antipoliomyelitic (human convalescent) serum many dire results can be prevented. Also careful treatment during the second stage of the disease will diminish immeasurably (90 per cent) the resulting deformities. He substantiated his observations with experimental work on monkeys.

Rhoads<sup>25</sup> injected intracerebrally into a monkey the virus of poliomyelitis which had been preserved in glycerol eight years. Eight days later there were marked symptoms of extensive involvement of the central nervous system. The animal was killed the following day, and marked degeneration of the anterior horn cells was demonstrated. The virus from the first monkey was passed through four other monkeys in succession and in all the disease developed without the virus losing any of its potency. The longevity of the virus suggests to Rhoads the improbability of the streptococci as the inciting organism in the disease.

Stewart and Rhoads<sup>26</sup> inoculated eight monkeys intradermally with repeated small doses of living active poliomyelitis virus. A second group of eight monkeys were given repeated small inoculations of the same virus subcutaneously. The period of immunization lasted from three to five months. During this period no signs suggesting poliomyelitis were found. The monkeys were bled and the neutralizing power of the serum on poliomyelitis virus was noted. Subsequently the monkeys were given intracerebral injections of poliomyelitis virus. The serums of all the monkeys, with the exception of one in which subcutaneous injection had been attempted, completely neutralized the virus. The degree of immunity was only relative, since one case immunized intradermally and four of the cases immunized subcutaneously exhibited definite poliomyelitis. The authors stated the belief that a greater degree of immunity is conferred by intradermal than by subcutaneous injections.

#### PYOGENIC INFECTIONS

Phemister<sup>27</sup> in discussing chronic fibrous osteomyelitis described the roentgenologic and microscopic appearance of such lesions in the early

24 Divelev, R. L. J. Bone & Joint Surg. **11** 100 (Jan.) 1929.

25 Rhoads, C. P. J. Exper. Med. **49** 701 (April) 1929.

26 Stewart, F. W. and Rhoads, C. P. J. Exper. Med. **49** 959 (June 1) 1929.

27 Phemister, D. B. Ann. Surg. **90** 756 (Oct.) 1929.



intermediate and late stages. He pointed out that during the first few months while the disease is progressive, the cavity is filled with soft, grayish or brown tissue and that microscopically it consists of fibroblasts, capillaries, polyblasts, giant cells and blood pigment. There is usually some necrosis about the cavity, and cholesterol slits are sometimes seen. The response about the fusion is variable, for a little or a great deal of new bone may be laid down. After a period of months or years the disease may come to a standstill, and the cavity may be partially or wholly filled with connective tissue or bone trabeculae bearing much resemblance to a benign giant cell tumor or an osteitis cystica.

These cases are usually not seen until they have been in progress for several months, because they are relatively symptomless. The organism is usually of low virulence. Eleven cases have been studied by Phemister, and he reported six of these.

#### ARTHRITIS

Current comment in the *Journal of the American Medical Association*<sup>28</sup> says that Poston<sup>29</sup> after the lapse of fifteen years during which he used the same technic as Rosenow, has isolated organisms from the glands removed from patients with infectious arthritis. She obtained growths from 72 of 120 glands, and 93 per cent of the organisms isolated were *Streptococcus viridans*. The similarity between the results of the pioneer work and those of the recent work will be of interest to the many physicians who at present are devoting their attention to the problems of arthritis.

An editorial in the *Journal of the American Medical Association*<sup>30</sup> says that Cecil and his co-workers strongly favor the view that chronic infectious arthritis is a streptococcal infection, caused, in a large proportion of cases, by a biologically specific strain of this organism. The demonstrated presence of this specific strain of streptococcus in the blood of several patients with advanced arthritis deformans goes far to corroborate the view already widely held that arthritis deformans and chronic infectious arthritis are one and the same disease. Whether the demonstrated micro-organisms act further, as some physicians believe, to exert an indirect physiologic influence through action on the endocrine systems remains far more problematic.

The results may indicate that etiologically there are at least two types of chronic arthritis—that which is a true specific infection char-

28 Cultures of Lymph Nodes in Arthritis, current comment, *J A M A* 93 1313 (Oct 26) 1929

29 Poston M A Gland Cultures in Infectious Arthritis *J A M A* 93 692 (Aug 31) 1929

30 Chronic Infectious Arthritis editorial, *J A M A* 93 284 (July 27) 1929

identified it traces by a definite cause and that which enters into the bacterial nature of does not have periods of bacteremia respectively into the present pathologic types of atrophic or hypertrophic arthritis on the one hand and hypertrophic arthritis on the other.

Cecil and his co-workers<sup>31</sup> reported the results of a series of blood and synovial fluid or membrane cultures in chronic arthritis. Blood cultures were obtained from seventy-eight patients. In forty-eight of these a streptococcus was found. There appeared to be a higher percentage of blood cultures in patients more than 50 and in those who had had the disease a number of years. In six cases cultures were made from synovial membrane, in one case culture was made from the synovial fluid. In five of these seven cases a bacterium was isolated, four showed a streptococcus. Eleven rabbits were given intravenous injections of these cultures, seven developed arthritis but only after repeated injections.

[Ed. Note.—These editorials show the strong trend toward a bacterial cause for all infectious arthritis. We doubt if the differentiation is as clean-cut as the editorial would lead us to believe.]

#### NEOPLASMS

Bucy<sup>32</sup> described the pathologic observations in seven cases of hemangioma of bone. Usually there is a hard swelling of bone over the area of the hemangioma. Microscopically, a vascular tissue is found, usually soft often of jelly-like consistency. It consists of large cavernous spaces containing blood cells and lined by a single layer usually of flat endothelium. There is a loose connective tissue stroma. The surrounding bony trabeculae show degenerative and formative changes which are probably secondary reactive phenomena. There is no microscopic evidence of a malignant condition. These growths may be called neoplasms or vascular malformations. The author can suggest no etiology from this study.

#### CIRCULATORY AND NERVE DISTURBANCES

Barron and Linenthal<sup>33</sup> concluded from their observations on thirty-four cases of thrombo-angitis obliterans, twenty-seven of which had come under their personal observation, that the disease is apt to be more generalized than commonly supposed, and that it may affect the vessels of the brain, heart and abdomen as well as those of the extremities.

31 Cecil, R. L., Nicholls, E. E., and Stainsby, W. J. Bacteriology of Blood and Joints in Chronic Infectious Arthritis, *Arch. Int. Med.* **43** 571 (May) 1929.

32 Bucy, P. C. *Am. J. Path.* **5** 381 (July) 1929.

33 Barron, M. E., and Linenthal, H. Thrombo-Angitis Obliterans. *Arch. Surg.* **19** 735 (Oct.) 1929.

Many of their patients, although they were all well under 50 years of age, suffered from hemiplegia, coronary disease or severe abdominal pain from arterial occlusion before or after the disease had manifest itself in the extremities. They believed that the disease is slow in onset, that the occlusion is primarily an inflammatory affair and that as it is developing there is opportunity for development of collateral circulation.

Kornblum<sup>34</sup> discussed the roentgen observations in the bones of the extremities in patients suffering from Raynaud's disease. The first changes are those of atrophy of bone in the affected phalanges with a gradual disappearance of the distal end of the phalanx. If the disease progresses, the entire phalanx may disappear. With recovery from the disease, there is disappearance of atrophy of the bone, and the phalanges again become visible in the roentgenograms. These changes have been observed in other conditions and are in no way pathognomonic of Raynaud's disease, but the author believes that they are evidence of tissue starvation from inadequate blood supply.

Two cases of loose intervertebral cartilage were reported by Dandy<sup>35</sup>. Both occurred in the lumbar region and followed rather mild trauma. Both cases presented marked symptoms of cord compression with extensive paralyses and loss of sphincter control. In both the roentgenogram was negative. In both the fragment of the cartilage was found lying loosely between the third and the fourth vertebral bodies and was pushing directly back against the dura. In each case the fragment was easily removed, and in each case recovery was progressive, although somewhat slow in the second case because of the relatively long duration of symptoms.

[ED NOTE—The rupture of intervertebral disks has been described before, but we feel that it is altogether probable that such a condition may exist more often than we are able to discover.]

#### SPINAL FUSION OPERATIONS IN THE TREATMENT FOR PAIN IN THE LOWER PART OF THE BACK AND FOR SCIATIC PAIN

A study was made by Chandler<sup>36</sup> of twenty-nine patients with pain in the lower part of the back and with sciatic pain on whom various types of spinal fusion operation had been performed. In eleven of the patients the fusion was of the lumbosacral region of the spine, and in one additional case the right sacro-iliac joint was fused at the same time. In the remaining seventeen patients, the author's operation of trisacral fusion

<sup>34</sup> Kornblum, K. *Am J Roentgenol* **21** 448, 1929.

<sup>35</sup> Dandy, W. E. Loose Cartilage from Intervertebral Disk Simulating Tumor of Spinal Cord. *Arch Surg* **19** 660 (Oct.) 1929.

<sup>36</sup> Chandler, F. A. Spinal Fusion Operations in Treatment of Low Back and Sciatic Pain. *J A M A* **93** 1447 (Nov. 9) 1929.

of the lumbosacral and both sacro-iliac joints had been done. In nine cases the results were entirely satisfactory to the patients but could not be rated as more than good because of some discomfort on certain motions of the spine. Two patients showing generalized arthritic changes obtained fair relief. Two patients showed no improvement in symptoms after lumbosacral fusion and their cases were considered failures. Fifteen patients reported complete relief from symptoms, and the results were considered excellent from the standpoint of both the patient and the surgeon. In regard to symptoms before operation the author stated that in general the objective manifestations of the pain in the lower part of the back were such as to indicate disease of the various elements of the spine and pelvis but lacked the clearcut differential features so frequently found in acute lesions of this region. Roentgenologic considerations were of the highest importance when interpreted in conjunction with the history and physical examination in determining the operation.

Phelps and Lindsay<sup>37</sup> reported that they had employed with success a slight modification of Verral's method of extra-articular fusion of both sacro-iliac joints in three patients. All obtained relief from their symptoms and were back at work within a year of their operation. The operation consisted in passing a bone graft which was removed from the tibia transversely through drill holes which were made in either posterior superior spine and through the spinous processes of the sacrum.

[ED. NOTE—Chandler's report is of considerable interest and shows the feasibility of relieving many patients with obstinate pain in the back by fusion operations. At the same time it is to be noted that results which could be rated as really excellent were obtained in only fifteen of twenty-nine cases, although improvement was noted in others. This would seem to argue for the need of careful study, accurate diagnosis and extreme conservatism before resorting to operation.]

*Operative Correction of Coxa Vara*—Heydemann<sup>38</sup> described the operative procedures that were employed for the treatment of coxa vara in Gocht's clinic in Berlin. In patients with mild deformities simple subtrochanteric osteotomy was considered sufficient. In cases of severe deformity, a cuneiform osteotomy was performed between the trochanters. The upper limb of the wedge was made in the direction of the axis of the neck of the femur. The size of the wedge to be removed was determined beforehand by careful measurement on the roentgenogram. The lower limb of the osteotomy was therefore made in accordance with these measurements. The inner cortical surface of the bone

<sup>37</sup> Phelps, W. M. and Lindsay, M. K. *Surg. Gynec. Obst.* **49**: 555 (Oct.) 1929.

<sup>38</sup> Heydemann, H. *Klin. Wchnschr.* **7**: 2250 (Nov. 18) 1928.

was not cut but left to be fractured when the osteotomized surfaces were approximated. Position was maintained by the application of plaster of paris spica casings. The advantages of the method were that the correction was made close to the seat of deformity, that it did not involve the joint, that damage to muscles was avoided and that the wide bony surfaces could be readily approximated. The results had been excellent in the patients treated, the gait had been improved, and Tiendelenburg's phenomenon had disappeared.

*Osteoplastic Surgical Exposure of the Ankle Joint*—Koenig and Schaefer<sup>39</sup> described a method of surgical approach to the ankle joint which had proved useful in their hands. A convex incision with its base downward was made over the internal malleolus. With an osteotome the malleolus was divided at its base, the deltoid ligament being preserved intact. It was then possible to dislocate the astragalus outward with the malleolus and expose the joint surfaces. In closing the incision, the malleolus was replaced and fixed with a nail. The method was suitable for fracture dislocations of the astragalus and other traumatic conditions and also for arthrodesis.

[ED. NOTE—This method of approach seems neat and under certain conditions ought to be useful.]

*Arthrodesis of the Ankle Joint*—Campbell<sup>40</sup> described the operative procedure he employed to secure osseous fusion of the ankle joint and reported the results obtained in three patients with tuberculosis and one with arthritis. Instead of denuding the cartilage from the articular surfaces of the ankle joint, he preferred to fuse the joint by making anterior and posterior incisions through which osteoperiosteal grafts were slid downward from the tibia into the denuded neck of the astragalus and upward from the os calcis into the denuded posterior borders of the astragalus and tibia. A plaster casing was worn for three months, followed later by a brace which was worn until the fusion was solid.

#### FRACTURES

*General*—Ashhurst<sup>41</sup> in discussing the question of whether accurate reduction of fracture is necessary, stated that generally speaking much less accurate reduction is necessary in children than in adults. Fractures into or near joints should always be replaced as accurately as possible. He said, further, that too much damage was frequently done to soft parts in attempting to secure accurate reduction of fractures of the shafts of bones that in such fractures, if bony union was obtained

<sup>39</sup> Koenig, F., and Schaefer, P. *Ztschr. f. Chir.* **215** 196, 1929.

<sup>40</sup> Campbell, W. C. *Am. J. Surg.* **6** 588 (May) 1929.

<sup>41</sup> Ashhurst, A. P. C. *Ann. Surg.* **90** 556 (Oct.) 1929.

and the axis of the fragment preserved and if there was shortening of not more than 1 cm. the result was usually satisfactory.

Stating his views on the operative treatment of fractures of the long bones, Scudder<sup>42</sup> enumerated the types of fractures which should frequently or always be treated by open reduction and described under what conditions such a procedure should be undertaken. He stated further that the ultimate aim in the treatment of any fracture should be a good functional result, that at times the anatomic result might be fair or poor yet the function of the joints good. Nevertheless unless conditions contraindicate it a perfect anatomic result should be striven for irrespective of whether it could be gained by closed or open methods.

Darrach<sup>43</sup> listed the dangers from the operative treatment for fractures as follows: (1) infection, (2) hemorrhage immediate or remote, (3) vascular interference resulting in delayed healing or nonunion, (4) faulty material—poor plaster or paris bandages defective plates or screws or weak suture material, (5) delayed decision i.e. operative treatment as a last resort and (6) faulty judgment.

*Fracture of the Internal Epicondyle of the Humerus with Displacement into the Elbow Joint*—Cotton<sup>44</sup> reported three instances of avulsion of the epiphysis of the internal epicondyle complicating dislocations of the elbow in which disturbance of the motor and sensory function of the ulnar nerve followed attempts at reduction. In each of the cases the fragment of bone was found lying in the elbow joint and tight bands of fascia from the displaced epiphysis were found pulling on the ulnar nerve. The treatment consisted in removal of the displaced fragment and release from tension on the ulnar nerve. Practically complete restoration of nerve function resulted in all cases. The author stated that he had seen twelve instances of this injury.

Brentnall<sup>45</sup> reported the operative results in two patients who had sustained fractures of the internal epicondyle of the humerus with displacement of the fragment into the elbow joint where it blocked movement. Both cases were unusual because there was no associated lesion of the ulnar nerve and the elbow had not been dislocated. This was contrary to the views of Cotton and of Fairbank both of whom believed that the displacement of the epicondyle was due to the manipulation of a dislocated elbow in the attempt to secure reduction. Brentnall suggested that the injury was caused by an abduction strain and was in reality a rupture of the internal lateral ligament of the elbow.

42 Scudder C. L. *Ann Surg* 90: 589 (Oct.) 1929.

43 Darrach W. *Ann Surg* 90: 595 (Oct.) 1929.

44 Cotton, F. J. *J. Bone & Joint Surg* 11: 348 (April) 1929.

45 Brentnall E. S. *Brit M J* 1: 1113 (June 22) 1929.

*Lesions of the Ulnar Nerve in Injuries of the Wrist*—In a group of 500 cases of injuries of the wrists, R. Watson Jones<sup>46</sup> found only three instances of palsy of the ulnar nerve. In one the injury was an outward dislocation of the wrist with a marginal fracture of the radius, and the palsy was due to traction on the nerve. The other two were due to contusion of the nerve, in the first the injury was a displacement of the radial epiphysis backward and outward with a radio-ulnar dislocation, and the nerve was impaled on the lower end of the diaphysis of the radius, which had gone forward and inward. In the second, the injury was an unreduced severe Colles' fracture, five weeks old, the nerve was impaled on the lower end of the upper fragment of the radius. The patients in all three cases recovered after reduction of the dislocations.

*Position in the Treatment for Fracture of the Carpal Scaphoid*—Berlin<sup>47</sup> made an anatomic study of the scaphoid bone, dissecting sixty wrists in order to determine what was the best position in which to treat fractures of the scaphoid. He found that the major portion of the ligamentous structure springing from the dorsal carpal ligament gained insertion on the proximal two thirds of the dorsal surface of the scaphoid bone. Since the dorsal carpal ligament was placed under tension with the hand in flexion the scaphoid ligamentous slip springing from it was likewise rendered taut and pulled the proximal fragment away from the distal one.

The approximation of the broken fragments was distinctly favored by the tendons of the flexor carpi radialis and the flexor pollicis longus. They acted together as a sling to the scaphoid bone on its volar surface when the hand was placed in extension.

The small lateral interosseous ligament in the proximal row of carpal bones was placed under tension when the hand was flexed to either side and in a minor degree displaced the fragment by tending to produce lateral angulation.

The radial collateral ligament stretching from the radial styloid to the tubercle of the scaphoid, by the nature of its attachment favored better alignment of fragments when the hand was extended to the radial side.

The position of choice in the treatment for carpal scaphoid fractures was about 45 degrees extension of the wrist with radial deviation avoiding extreme or forced extension.

[ED. NOTE.—Berlin's observations confirm what had already been established by clinical results that a position of moderate dorsiflexion of the wrist gives the best approximation of fragments in scaphoid fractures.]

46 Jones, R. Watson. *Proc. Roy. Soc. Med.* **22** 1071 (June) 1929.

47 Berlin, D. *New England J. Med.* **201** 574 (Sept. 19) 1929.

*Fracture Dislocations of the Cervical Spine*—Three instances of fracture of the atlas were reported by McWhorter<sup>48</sup> all occurring in adult males. In two of the patients the injury was produced by a fall on the head, in the third case the patient was struck by an automobile. In only one patient was the atlas alone involved. In this case the ununited posterior arch was removed three months after injury to relieve a severe occipital neuralgia. Complete recovery followed the operation. The author reviewed the literature.

Taylor<sup>49</sup> discussed fracture dislocations of the cervical vertebrae, particularly those produced by indirect violence and dealt with the methods of production and the various types of injury that might be sustained by the cord, the spinal nerves and the cervical spine and its supporting structures. He advised manual traction under a general anesthetic as a means of reducing the fracture dislocation followed by the application of a plaster jacket with a head piece to be worn for several weeks—followed later by physiotherapy. Illustrative cases were appended.

*Vertebral Fractures Without Spinal Deformity and Without Lesions of the Spinal Cord*—Huet<sup>50</sup> made a comprehensive study of vertebral fractures without associated lesions of the spinal cord. He pointed out their great frequency and the difficulty of recognizing them from clinical signs alone. The traumatism was often slight. A fall or blow on the head or the neck usually caused cervical injuries while fractures of the lower lumbar region resulted most commonly from falls on the feet or on the ischia in the sitting position. The dorsal region of the spine was better protected by reason of the greater strength of the anterior common ligament at this level and this explained the relatively lesser frequency of injuries here.

Displacement of the fragments might be almost nil but in the majority of cases was more or less marked. Usually it was produced immediately at the moment of injury, but it might occur secondarily during transportation or late as in the case of the progressive displacement observed in patients with unrecognized and untreated fractures. A long period was required for the production of firm bony callus, and hence prolonged immobilization in good position was necessary to prevent increase in the bony deformity.

From the standpoint of industrial and legal medicine it had to be recognized that the period of temporary disability was of long duration, in the case of cervical injuries. Stempel and Boekel estimated it at about one year. Even though this might seem long to insurance companies it

48 McWhorter G L. *J Bone & Joint Surg* **11** 285 (April) 1929

49 Taylor A S. *Ann Surg* **90** 321 (Sept.) 1929

50 Huet M P. *J de chir* **34** 15 (July) 1929



was to their interest not to attempt to shorten it. Insufficient treatment was likely to be followed by unpleasant sequelae, such as crumpling of the vertebral body, development of exostoses, delayed involvement of the cord, paralysis, etc. The disability that resulted even in cases of slight fracture due to complaint of pain was not less than 10 per cent and more often was from 20 to 40 per cent and even higher.

Discussing the relations between these lesions and Kummel-Verneuil's disease, the author expressed the opinion that Kummel's syndrome did not exist. In France, the case described by Robineau in which the integrity of the vertebra had been shown by a roentgenogram made immediately after the injury, remained unique.

[ED NOTE—This article is of value in recording French opinion on the subject of vertebral fractures.]

*Injuries Complicating Fractures of the Pelvis*—Wakeley<sup>51</sup> recorded the complications associated with 100 nonfatal cases of fractures of the pelvis. Of these, only eleven were complicated by visceral injuries: six, rupture of the urethra, four, extraperitoneal rupture of the bladder and one, intraperitoneal rupture of the bladder. In no nonfatal case was the rectum injured. All these complications were associated with "run-over" accidents, nonfatal accidents, the result of direct trauma and of crushing forces were not complicated by visceral injuries. There was no case of injury to the sacral nerves at the time of the injury, and only one at a later date, following a fracture of the sacrum, and due possibly to compression from excessive callus formation.

*Perforating Fractures of the Acetabulum*—Cottalorda<sup>52</sup> made a study of perforating fractures of the acetabulum, basing his conclusions on a review of the literature and an analysis of one hundred and seven reported and unreported cases. The injury was encountered most commonly in men between the ages of 20 and 40 years. In the majority of cases it was caused by a fall on the lateral surface of the greater trochanter, the hip being in a position of extension and of extreme internal rotation. The author reviewed the symptomatology and pointed out that rectal examination rarely gave clear information as to the nature of the injury in spite of the fact that it was generally considered to be pathognomonic. He recognized three types of deformity: fractures without penetration, fractures with partial penetration and fractures with complete penetration.

Regarding the fracture from the industrial point of view he distinguished on a clinical basis three types of old fracture: first, the pseudo-coxalgic type, second the dystocic or obstetric type, and third, the progressive type in which the protrusion of the femoral head into the

<sup>51</sup> Wakeley, C. P. G. *Brit. J. Surg.* **17**: 22 (July) 1929.

<sup>52</sup> Cottalorda, I. *Presse med.* **37**: 388 (March 23) 1929.

pelvis begins and increases progressively by reason of premature use. It happened however, even with a marked penetration of the femoral head that the patient sometimes developed an adaptation to the condition and was able to take up his former employment. The most common complications were rupture of the bladder and urethra, hematoma under the psoas muscle and stubborn neuralgias.

The prognosis was the more serious the greater the degree of penetration of the head. Twenty-seven of eighty-six patients were reported as cured (31.3 per cent), twenty-four or 27.9 per cent died, and in thirty-five or 40.6 per cent varying degrees of ankylosis developed. The percentage of disability was estimated at between 30 and 40 per cent, and the average period of time required for consolidation was six months.

*Treatment for Fractures of the Leg by Delbet's Plaster Splint*—Crossan<sup>53</sup> advocated the use of the Delbet plaster splint for the treatment for fractures of the middle and lower thirds of the leg and reported the results of such treatment. In ninety-nine patients with such fractures admitted to Ashburt's service at the Episcopal Hospital in Philadelphia between October, 1922 and October, 1927, all but thirty-three were treated by this method. Fifty-two of these patients were traced and a study of the end-result obtained. Forty-three, or 83 per cent, showed a good anatomic result, 13 per cent a fair and 4 per cent a poor result. The function in forty-four cases, or 85 per cent, was good, in 11 per cent fair and in 4 per cent poor.

The materials necessary and their application to make the Delbet splint were described. It was applied while continuous traction over the end of the table was maintained. The patient was made to walk in ten days with crutches, and in six weeks the plaster was removed.

#### DISLOCATIONS

*Dislocations of Semilunar Bone*—Discussing dislocations of the carpal semilunar bone, Watson-Jones<sup>46</sup> analyzed the end-results in twelve patients whom he had treated. In two this bone was excised, giving a 75 per cent return of function, in the third the semilunar and half the scaphoid were excised, with a 50 per cent return of function. Six patients were seen within a few days of the injury and the dislocation was reduced by closed manipulation, with a 100 per cent return of function.

Watson-Jones described his method of closed reduction as follows:

The patient's wrist was fully dorsiflexed, the thumb of one hand was placed anteriorly over the dislocated bone to steady it and to prevent it rotating forward.

<sup>53</sup> Crossan, E. T. Delbet Apparatus and End-Results. Arch. Surg. **19**: 712 (Oct.) 1929.

With the other hand the manipulator gripped the patient round the fingers, exerted strong traction, and pulled the os magnum away from the radius. Whilst exerting this traction the hand was slowly palmar flexed, the os magnum was gradually pulled round the back of the semilunar until its head glided into the cup of the bone.

This maneuver was unsuccessful when injuries were more than four days old, and for those Watson-Jones advocated open reduction, through a 3 inch dorsal incision, the head of the os magnum was freed from the adhesions which had formed between it and the capsule and the remaining bones, then the same maneuver was employed as in the closed method of reduction to secure replacement. Watson-Jones was strongly opposed to the method of reduction in which the semilunar is pried back into position by means of bone levers.

Three patients on whom open reduction by the author's method had been done were back at work: one as a ship's riveter, another as a sailor and the third as a railway engine driver.

Watson-Jones thought that closed reduction should be attempted up to the end of a week after the injury, open reduction thereafter and excision not unless the injury was of more than three months' duration.

*Utilization of Long Tendon of Biceps to Prevent Recurrent Dislocation of the Shoulder*—Nicola<sup>54</sup> described a new operation for recurrent dislocation of the shoulder in which he utilized the long tendon of the biceps muscle to serve as a check ligament. He divided the tendon 1½ inches (3.8 cm.) above the point where it dipped down to pass under the pectoralis major muscle, freed the proximal end well up into the bicipital groove and passed it through a tunnel drilled in the head of the humerus to be resutured at the point where it emerged to the divided distal end of the tendon. The arm with the elbow flexed to an angle of 45 degrees was bandaged to the side for three weeks, after which active use was permitted.

*Reduction of Dislocations of the Hip Under Nerve Block Anesthesia*—Mueller<sup>55</sup> stated that he had found that manipulative reduction of traumatic dislocations of the hip, which was always difficult under general anesthesia, was greatly facilitated by nerve block anesthesia. He had employed paravertebral nerve block of the first to the fourth lumbar roots and infiltration of the sciatic nerve. He had used it in four cases with complete success. In one of the patients reduction had been tried under general anesthesia by three different surgeons the day previously. In another patient the reduction was accomplished almost spontaneously, after anesthesia had been secured, by turning the patient from the prone into the supine position.

<sup>54</sup> Nicola T. Am J Surg 6:815 (June) 1929.

<sup>55</sup> Mueller W. Zentralbl f Chir 57:224 1930.

The author had likewise made use of nerve block of the brachial plexus in cases of dislocation of the humerus. Here too he had found that reduction was made remarkably easy.

[ED NOTE—The muscular relaxation obtained by nerve block is more complete than with general anesthesia and thus the muscular resistance which has to be overcome in securing reduction is diminished or eliminated. There would seem to be a real advantage in the method, particularly in dislocation of the hip.]

#### RESEARCH

*Influence of Irradiation on the Resistance to Infection*—With a view to determining the influence of irradiation on resistance to infection Eidinow<sup>56</sup> carried out experiments on animals. He irradiated a group of rabbits with his special lamp (emitting infra-red luminous and ultra-violet rays up to 2850 angstrom units) continuously for forty-eight hours, and then inoculated them intravenously with a broth culture of virulent staphylococci. The control animals died within twenty-four hours of the inoculation, while four of the thirty irradiated animals recovered, and the remaining twenty-six survived for an average of seven days. Eidinow was unable to discover the mechanism of the increased resistance. Experiments indicated that the irradiation increased the hemobactericidal power but not in proportion to the general increased resistance to infection. It did not raise the rectal temperature.

*The Intra-Articular Pressure and Absorbing Power of Joints*—Rostock,<sup>57</sup> using a manometer, measured the intra-articular pressure in knee joints following injuries with effusion of blood. In some instances he found pressures as high as 700 mm. of water. The amount of intra-articular pressure was not directly proportionate to the amount of the effusion. The pressure was greatest immediately after the injury and diminished in time. As a result of his studies, Rostock was impressed with the importance of evacuating fluid as early as possible with the view of lessening the damage to the joint. Even when the fluid was not entirely removed aspiration lessened the intra-articular pressure, and hence reduced the danger of chronicity. Measurements of the pressure in joints with septic arthritis showed particularly high readings.

The same author<sup>58</sup> also studied the absorbing power of the knee joint in more than 100 patients with different disease conditions. He injected a known quantity of sodium iodide solution and then measured the amount of iodine excreted in the urine during a given time. He found that the rate, amount and duration of the absorption varied

<sup>56</sup> Eidinow, A. Brit. M. J. **2**: 293 (Aug. 17) 1929.

<sup>57</sup> Rostock, P. Deutsche Ztschr. f. Chir. **213**: 314 1929.

<sup>58</sup> Rostock, P. Deutsche Ztschr. f. Chir. **215**: 76 1929.

markedly in different diseases and under different conditions. In septic arthritis the absorption was rapid and of large amount, especially during the first hour following injection. The absorption when infection was absent was far less rapid. The rate of absorption in traumatic conditions with hemarthrosis varied with the duration of the condition, it was most rapid when the injury was recent. A slow beginning and a long duration were noted in chronic hydrops. Because of the sluggish rate in chronic joint conditions, Rostock considered it advisable to perform arthrotomy with the purpose of creating an acute condition and thus speeding absorption.

[ED NOTE—Rostock's experiments are of interest as tending to shed further light on the physiology of joints under diseased conditions. Further studies under normal and abnormal conditions will be necessary before their true significance can be appraised.]

*Experimental Arthritis*—Key<sup>59</sup> studied the reaction of the knee joints in rabbits to single and repeated injections of citrated blood and to single injections of india ink. The cells were studied by fixed smears and by vital staining methods, followed at the end of twelve days by microscopic study of the joint tissues. A single injection of citrated blood produced a cellular exudate, which disappeared in about twelve days. During the first two days, leukocytes were the predominating cells, later, macrophages predominated. The only change in the exudate with repeated injections was an increase in the number and size of the macrophages. With injections of india ink, the exudate contained many leukocytes and macrophages throughout the twelve day period. The majority of the macrophages were monocytes. Some red blood cells in the exudate were carried away by clasmotocytes, others were entangled in fibrin clots which became organized and covered by synovial lining cells. Most of the india ink was removed by macrophages and leukocytes, some was organized in fibrin clots and covered by synovial lining cells. With single injections of india ink or citrated blood there was a mild proliferation of the surface cells and infiltration of the subsynovial tissues with leukocytes and macrophages. With repeated injections of blood the synovial membrane was markedly thickened. No observations were made after the twelfth day. At this time the tissues showed a partial return to the normal condition.

*Experiments with Foreign Materials to Stimulate Epiphyseal Growth of Long Bones*—Bohlman<sup>60</sup> reported experiments performed with foreign materials in the region of the epiphyseal cartilage plate to stimulate longitudinal growth of bones. Pegs of various metals, wood, ivory,

59 Key J A J Bone & Joint Surg **11** 705 (Oct) 1929

60 Bohlman H R J Bone & Joint Surg **11** 355 (April) 1929

autogenous bone insoluble salts essential oils and vaccines were used as foreign materials. The author concluded that there was no increased growth in length of bone in any of the animals. In many cases, a marked shortening resulted.

*The Vessel Canals in Normal Bone*—From the studies of the development of the vessel canals Joffe<sup>61</sup> pointed out that in fetal bone the vessels grew in from the periosteum. The spaces between the periosteal trabeculae constituted the primary haversian systems. In early infancy canals were present in the cortex and connected the haversian canals and the marrow cavity. In the epiphyses canals were present which disappeared as cartilage was replaced by bone. By the eleventh year the adult vessel pattern was found. Before this age there were reconstructions of the vessels in the bone old ones being obliterated and new ones laid down. The haversian canals ran longitudinally. Those nearer the surface communicated with canals of the ground lamellae which in turn anastomosed with periosteal vessels. The Volkmann's canals were formed by canalization of fully developed bone by new vessels which entered the bone at various angles to its long axis.

#### MISCELLANEOUS

*Disease of the Temporomandibular Joint*—One of the chief obstacles to the diagnosis of and treatment for lesions of the temporomandibular joint is the difficulty of showing the region clearly in the roentgenograms. Bishop<sup>62</sup> made a study of the normal and pathologic anatomy of this articulation and of its varying appearance in the roentgenogram. He described a method of making a roentgen examination of the joint which minimized distortion and ought to lead to more accurate diagnosis.

Wakeley<sup>63</sup> reported his operative observations on two patients with displacement of the mandibular cartilage. In both the cartilage preserved only its anterior attachment the posterior attachment having been torn. Both patients complained of an audible click on mastication. In one the symptoms followed a violent fit of coughing and in the other the extraction of a tooth under anesthesia. The click disappeared after the removal of the cartilage.

*Fixed Obliquity of the Pelvis*—Mayer<sup>64</sup> stated that fixed obliquity of the pelvis might result from (1) contraction of the hip abductors on one side, (2) contraction of the hip abductors on one side combined with contraction of the adductors on the opposite hip, (3) a combina-

61 Joffe H. L. *Am J Path* 5 323 (May) 1929

62 Bishop P. A. *Am J Roentgenol* 21 556 (June) 1929

63 Wakeley, C. P. *Lancet* 2 543 (Sept 14) 1929

64 Mayer L. *Am J Surg* 6 804 (June) 1929

tion of the first and second plus contracture of the spinal muscles producing fixed deformity of the lumbar spine

In recent cases traction might suffice to correct the deformity. In cases of long standing, operative treatment was necessary. This consisted of complete division of the tensor fascia femoris and abduction of the muscles and of the capsule of the hip joint through a lateral incision. To maintain the hip in adduction, a strip of fascia lata was freed above the knee and dissected upward to a point midway between the hip and knee and then carried subcutaneously over the anterior thigh and sewed to the pubic spine. It might be necessary to divide the adductors of the opposite hip and if the spinal muscles were contracted, traction ought to be applied to the spine.

[ED. NOTE.—Fixed obliquity of the pelvis is a troublesome problem and in our experience has not been especially helped by the usual methods of scoliotic correction. Mayer's method sounds radical but we shall watch his results with interest.]

*Morbus Coxae Senilis*.—Kienbock<sup>65</sup> explained the development of deforming osteo-arthritis of the hip on the basis of a premenstrual trophostatic change in the structures composing the joint. The primary changes were caused by nutritive disturbance, and secondary static changes then occurred. The initial signs shown by roentgen examination were depression of the acetabular roof and elongation of the lateral rim. With this there would be noticed a certain amount of osteoporosis. The primary changes did not occur in the head but in the acetabulum. The condition might remain stationary at this state or progress with the development of the characteristic deformity. He distinguished a primary and secondary type, the latter being the result of earlier lesions of the hip such as accidents or Calve-Legg-Perthe's disease.

*Intrapelvic Protrusion of the Acetabulum*.—Doub<sup>66</sup> reported eight cases of intrapelvic protrusion of the acetabulum. It was bilateral in five cases and unilateral in three. The duration of symptoms was from one to seven years, with an average of three and one half years. Clinically, the most common observation was restriction or absence of abduction of the leg and next was restriction of flexion and hyperextension. The ages varied from 16 to 53. The roentgenograms showed a deepening of the acetabulum with thinning of the mesial and inferior wall. The head of the femur was, therefore, more deeply buried, and the greater trochanter was somewhat higher and closer to the ilium. As to the etiology he suggested that the condition could best be explained by some general disease in early life causing softening of the bones with resulting deformity, and that the osteo-arthritis so often found was a later stage in the process.

<sup>65</sup> Kienbock, R. *Med. Klin.* 25: 817 (May 24) 1929; 25: 860 (May 31) 1929.

<sup>66</sup> Doub, H. P. *Radiology* 12: 359 (May) 1929.

*A Study of Fitting the Ring of the Thomas Splint*—Those interested in the careful fitting of Thomas splints would do well to consult Young's recent article which was based on a study of the living subject and of the cadaver. He concluded that the shape of the ring, its size, padding and other characteristics depended on the purpose for which the splint was to be used. The shape and angle should differ depending on whether the patient is recumbent or ambulatory or whether the hip is flexed much or little or is in a position of extension.

*Cysts of the Semilunar Cartilages*—The literature accumulating on cysts of the semilunar cartilages of the knee was further enriched by Ollerenshaw's report of eighteen additional cases. Of these, four were in connection with the internal cartilage. The author reaffirmed his belief that the cysts were of developmental origin. The pathologic histology was described and illustrated by several excellent photomicrographs.

*Pes Valgus Staticus*—Boehm<sup>67</sup> has continued his studies of the development of deformities of the knee and foot, comparing the conditions found with certain stages of the development of the lower extremities in the human embryo. His theories in regard to the development of clubfoot have been previously described. On the basis of additional observations he recently reported finding similar relationships in respect to pes valgus staticus meaning that form of pronated foot which is generally first noticed during the years of puberty and which has generally been explained on the basis of faulty statics. He found that the embryonic foot at a certain stage in its development showed certain similarities to the pronated foot of adolescence, especially in the relations between the axes of the tibioastragalar and subastragalar joints. This relation was different from that seen in the normal and rachitic pronated foot. This difference was shown by illustrations of the specimens. Boehm concluded that the occurrence of pes valgus staticus could be explained on the basis of an arrested development with permanent alteration of the planes of the articular surfaces.

Steindler,<sup>70</sup> studying the mechanics of pes valgus, observed that in most cases of nonrigid flatfoot there was a compensatory supination of the forefoot. This he explained as due to the necessity of securing plane contact of the entire forefoot with the floor. When the posterior portion of the foot was in a valgus position a supination of the forefoot had to occur at the midtarsal joint to permit weight-bearing over the

67 Young C S. Study in Fitting Ring of Thomas Splint. *J. A. M. A.* 93: 602 (Aug. 24) 1929.

68 Ollerenshaw R. *Brit. J. Surg.* 16: 555 (April) 1929.

69 Boehm M. *Ztschr. f. orthop. Chir.* 52: 424 1929.

70 Steindler A. *J. Bone & Joint Surg.* 11: 272 (April) 1929.



entire forefoot. He believed that in order to rebalance the foot it was necessary to insert not only a pronatory wedge under the inner side of the heel, but also a supinatory outer wedge under the little toe.

*Traumatic Subastragalar Arthropathy*—O'Connor<sup>71</sup> described a condition affecting the subastragalar joint following trauma, but without any demonstrable fracture, which he called traumatic subastragalar arthropathy. He had observed the condition in five patients. There was a history of long-continued pain and disability. In one patient subastragalar arthrodesis was performed with relief from symptoms. The symptoms consisted of pain in the heel on weight-bearing and inability to walk on rough ground without pain. On examination tenderness was found on pressure along the medial, lateral or both aspects of the subastragalar joint and pain in the subastragalar joint on hammer percussion over the heel or on attempting to rise on the ball of the foot or on lateral movement of the foot. He did not believe that the prognosis for recovery without pain was good under conservative treatment and expressed the opinion that subastragalar arthrodesis was indicated if the pain persisted after three months.

#### SURGICAL INTERVENTION IN DISEASES OF THE TENDONS, BONES AND JOINTS

*Present Status of Synovectomy*—Analyzing the present status of the operation of synovectomy, Swett<sup>72</sup> expressed the opinion that it has a definite place in certain cases of chronic infectious arthritis, particularly of the knee. The operation should be performed only after the elimination of foci of infection and the establishment of a good state of nutrition. In the patients on whom he had performed the operation there had been a good immediate response, but in several there had later been a relapse and subsequent involvement of other joints.

[**ED. NOTE**—We agree that synovectomy of the knee has a place, but rather a limited place, in surgical treatment for chronic arthritis. It is particularly beneficial in the patients with chronic hydrops. Its effects are much more local than general.]

71 O'Connor D. S. *New England J. Med.* **200**: 987 (Mar. 9) 1929.

72 Swett P. P. *Am. J. Surg.* **6**: 807 (June) 1929.

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